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NEWS	1		Web Page for STN Seminar Schedule - N. America
NEWS	2	MAY 01	New CAS web site launched
NEWS	3	MAY 08	CA/CAplus Indian patent publication number format defined
NEWS	4	MAY 14	RDISCLOSURE on STN Easy enhanced with new search and display fields
NEWS	5	MAY 21	BIOSIS reloaded and enhanced with archival data
NEWS	6	MAY 21	TOXCENTER enhanced with BIOSIS reload
NEWS	7	MAY 21	CA/CAplus enhanced with additional kind codes for German patents
NEWS	8	MAY 22	CA/CAplus enhanced with IPC reclassification in Japanese patents
NEWS	9	JUN 27	CA/CAplus enhanced with pre-1967 CAS Registry Numbers
NEWS	10	JUN 29	STN Viewer now available
NEWS	11	JUN 29	STN Express, Version 8.2, now available
NEWS	12	JUL 02	LEMBASE coverage updated
NEWS	13	JUL 02	LMEDLINE coverage updated
NEWS	14	JUL 02	SCISEARCH enhanced with complete author names
NEWS	15	JUL 02	CHEMCATS accession numbers revised
NEWS	16	JUL 02	CA/CAplus enhanced with utility model patents from China
NEWS	17	JUL 16	CAplus enhanced with French and German abstracts
NEWS	18	JUL 18	CA/CAplus patent coverage enhanced
NEWS	19	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS	20	JUL 30	USGENE now available on STN
NEWS	21	AUG 06	CAS REGISTRY enhanced with new experimental property tags
NEWS	22	AUG 06	BEILSTEIN updated with new compounds
NEWS	23	AUG 06	FSTA enhanced with new thesaurus edition
NEWS	24	AUG 13	CA/CAplus enhanced with additional kind codes for granted patents
NEWS	25	AUG 20	CA/CAplus enhanced with CAS indexing in pre-1907 records

NEWS EXPRESS 29 JUNE 2007: CURRENT WINDOWS VERSION IS V8.2,
CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

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FILE 'HOME' ENTERED AT 11:47:08 ON 20 AUG 2007

=>  file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 11:47:26 ON 20 AUG 2007

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=> s antibody production
L1       71694 ANTIBODY PRODUCTION

=> s l1 and high yield
L2         101 L1 AND HIGH YIELD

=> s l2 and framework modification
L3           0 L2 AND FRAMEWORK MODIFICATION

=> s l2 and modified
L4          12 L2 AND MODIFIED

=> s l4 and framework
L5           0 L4 AND FRAMEWORK

=> dup remove l4
PROCESSING COMPLETED FOR L4
L6           6 DUP REMOVE L4 (6 DUPLICATES REMOVED)

=> d l6 1-6 cbib abs

L6   ANSWER 1 OF 6     MEDLINE on STN
2006473807.    PubMed ID: 16896231.   Cosecretion of protease inhibitor
     stabilizes antibodies produced by plant roots. Komarnytsky Slavko;
     Borisjuk Nikolai; Yakoby Nir; Garvey Alison; Raskin Ilya. (Biotech Center,
     Rutgers University, New Brunswick, New Jersey 08901, USA..
     komar@aesop.rutgers.edu) . Plant physiology, (2006 Aug) Vol. 141, No. 4,
     pp. 1185-93.  Journal code: 0401224. ISSN: 0032-0889. Pub. country: United
     States. Language: English.
AB   A plant-based system for continuous production of monoclonal antibodies
     based on the secretion of immunoglobulin complexes from plant roots into a
     hydroponic medium (rhizosecretion) was engineered to produce high levels
     of single-chain and full-size immunoglobulins.  Replacing the original
     signal peptides of monoclonal antibodies with a plant-derived calreticulin
     signal increased the levels of antibody yield 2-fold.  Cosecretion of
     Bowman-Birk Ser protease inhibitor reduced degradation of the
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immunoglobulin complexes in the default secretion pathway and further increased antibody production to 36.4 microg/g root dry weight per day for single-chain IgG1 and 21.8 microg/g root dry weight per day for full-size IgG4 antibodies. These results suggest that constitutive cosecretion of a protease inhibitor combined with the use of the plant signal peptide and the antibiotic marker-free transformation system offers a novel strategy to achieve high yields of complex therapeutic proteins secreted from plant roots.

L6 ANSWER 2 OF 6 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

1998327532 EMBASE A recombinant soluble form of the integrin α(IIb)β3 (GPIIB-IIIa) assumes an active, ligand-binding conformation and is recognized by GPIIB- IIIa-specific monoclonal, allo-, auto-, and drug-dependent platelet antibodies. Peterson J.A.; Visentin G.P.; Newman P.J.; Aster R.H.. Dr. J.A. Peterson, Blood Research Institute, 8727 Watertown Plank Rd., Milwaukee, WI 53226-3584, United States. Blood Vol. 92, No. 6, pp. 2053-2063 15 Sep 1998.
Refs: 49.
ISSN: 0006-4971. CODEN: BLOOAW
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 19981109. Last Updated on STN: 19981109

AB The IIb-IIIa glycoprotein complex is a favored target for allo-, auto-, and drug-dependent antibodies associated with immune thrombocytopenia. A soluble, recombinant form of the GPIIb-IIIa heterodimer that could be produced in large quantities and maintained in solution without detergent could provide a useful experimental tool for the study of platelet-reactive antibodies, but previous attempts to produce such a construct have yielded only small quantities of the end product. Using a baculovirus expression system and the dual-promoter transfer vector P2Bac, we were able to express soluble GPIIb-IIIa complex (srGPIIb-IIIa) lacking cytoplasmic and transmembrane domains in quantities of about 1,000 μg/L, about 40 times greater than reported previously. The high yield achieved may be related to inclusion of the entire extracellular region of the GPIIb light chain in the construct. srGPIIb-IIIa reacts spontaneously with fibrinogen, and this interaction is totally inhibited by the peptide RGDS. Reactions of 24 GPIIb-IIIa-specific antibodies evaluated (12 monoclonal, 3 allo-specific, 3 auto- specific, and 6 drug-dependent) with srGPIIb-IIIa were indistinguishable from reactions with platelet GPIIb-IIIa. Thus, srGPIIb-IIIa spontaneously assumes an active, ligand-binding conformation and contains epitopes for all monoclonal and human antibodies tested to date. srGPIIb-IIIa can be produced in large quantities, can readily be modified by site-directed mutagenesis, and should facilitate identification of epitopes recognized by GPIIb-IIIa- specific antibodies, study of the mechanism(s) by which certain drugs promote antibody binding to GPIIb-IIIa in drug-induced thrombocytopenia and structure-function relationships of GPIIb-IIIa.

L6 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 1

88009184. PubMed ID: 3655377. Effect of feeding rate on monoclonal antibody production in a modified perfusion-fed fermentor. Velez D; Reuveny S; Miller L; Macmillan J D. (Department of Biochemistry and Microbiology, New Jersey Agricultural Experiment Station, Rutgers University, New Brunswick, NJ 08903.) Journal of immunological methods, (1987 Sep 24) Vol. 102, No. 2, pp. 275-8. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB Previously we described a perfusion system for production of high yields of monoclonal antibodies in a fermentor. This system incorporated a cylindrically shaped, stainless steel filter mounted around the stirring shaft for retention of cells within a 1 liter fermentor.

Modification of this filter by increasing the pore size from 5 micron to 10 micron decreased its tendency to clog and allowed continuous operation for about 3 weeks. Fresh culture medium, containing 6.5 mg glucose/ml and 3% horse serum, was supplied continually at two different perfusion rates, 850 and 1100 ml/day. Spent culture medium containing monoclonal antibody was harvested concomitantly. Highest cell density (5 X 10(7)/ml) and best antibody yield (1.7 g/l culture per day) were obtained at the higher feeding rate.

L6 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
1986:184775 Document No. 104:184775 Methods and cell lines for immortalization and monoclonal antibody production by antigen-stimulated B-lymphocytes. Kaplan, Henry S.; Teng, Nelson N. H.; Lam, Kit S.; Calvo-Riera, Francisco (Leland Stanford Junior University, USA). U.S. US 4574116 A 19860304, 6 pp. (English). CODEN: USXXAM. APPLICATION: US 1983-457795 19830113.

AB A method for efficiently producing human monoclonal antibodies by mouse-human heterohybridomas is described. An immortalized human myeloma cell line is modified by introducing a selectable dominant resistance marker. The resulting hypoxanthine-aminopterin-thymidine (HAT)-sensitive, selectable agent resistant human cell line is fused with a HAT-sensitive, immortalized mouse (or rat) myeloma cell line (which preferentially has been treated with chromosome-damaging agents, such as x-rays) and incubated in the presence of appropriate selection agents. The result is a high yield of viable mouse-human heteromyelomas in which ≥1 human chromosomes are stably retained. After cloning the most rapidly growing hybrid myeloma cells, the resulting HAT-sensitive hybrid cells may be fused with antigen-sensitized human B-lymphocytes for the stable production of human monoclonal antibodies.

L6 ANSWER 5 OF 6 MEDLINE on STN DUPLICATE 2
83266915. PubMed ID: 6409964. Improved conditions for the production of monoclonal antibodies to carcinogen-modified DNA, for use in enzyme-linked immunosorbent assays (ELISA). Hertzog P J; Shaw A; Lindsay Smith J R; Garner R C. Journal of immunological methods, (1983 Aug 12) Vol. 62, No. 1, pp. 49-58. Journal code: 1305440. ISSN: 0022-1759. Pub. country: Netherlands. Language: English.

AB The methodology for the production of monoclonal antibodies to chemical carcinogen-modified DNA has been improved to provide high yields of hybridomas, using guanine-imidazole ring-opened aflatoxin B1-modified DNA as an example (iro-AFB1 DNA). The percentage of immunised mice which responded to iro-AFB1 DNA-protein immunisation and the number of specific hybridomas produced was dependent on the level of modification of DNA. One in three BALB/c mice had detectable (but low) antibody titre when 0.3% modified iro-AFB1 DNA was used and this yielded 2 specific hybridomas, whereas all mice responded at reasonable titres and 6 specific hybridomas were obtained when 3% modified iro-AFB1 DNA was used. Other factors found to improve the number and titre of mice responding to immunisation and the yield of hybridomas were: KLH greater than BSA as carrier protein, C57 BL/6 X BALB/c F1 greater than BALB/c mice for antibody production, fusion success and ascites growth. The conditions limiting the sensitivity and reproducibility of an enzyme-linked immunosorbent assay (ELISA) using these monoclonal antibodies with beta-galactosidase-linked sheep F(ab')2 anti-mouse IgG as the second antibody were also tested. Present experience with AFB1 and other carcinogens indicates that these methods should be applicable to the production of monoclonal antibodies to DNA modified by a wide variety of chemical carcinogens.

L6 ANSWER 6 OF 6 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
1981:257486 Document No.: PREV198172042470; BA72:42470. SEPARATION OF M

PROTEIN FROM INFLUENZA VIRUS BY AGAROSE GEL ELECTROPHORESIS. LECOMTE J [Reprint author]; CROTEAU G. CENTRE DE RECHERCHE EN VIROLOGIE, INSTITUT ARMAND-FRAPPIER, 531 BLVD, DES PRAIRIES, LAVAL, QUEBEC H7V 1B7, CANADA. Journal of Virological Methods, (1981) Vol. 2, No. 4, pp. 211-222. CODEN: JVMEDH. ISSN: 0166-0934. Language: ENGLISH.

AB A simple procedure for obtaining a high yield of electrophoretically and immunologically pure M-protein from influenza virus by agarose gel electrophoresis is described. The electrophoretic pattern thus obtained is amenable to direct identification by a modified counter-immunoelectrophoresis procedure and by SDS[sodium dodecyl sulfate]-polyacrylamide gel electrophoresis. Antibodies can also be produced by injecting animals with protein-agarose complexes, bypassing any extraction procedures.

=> s l1 and modified framework
L7 0 L1 AND MODIFIED FRAMEWORK

=> s antibod?
L8 3011979 ANTIBOD?

=> s l8 and modified framework
L9 4 L8 AND MODIFIED FRAMEWORK

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10 4 DUP REMOVE L9 (0 DUPLICATES REMOVED)

=> d l10 1-4 cbib abs

L10 ANSWER 1 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2007:186053 Document No.: PREV200700192359. Immunocytokine sequences and uses thereof. Anonymous; Gillies, Stephen D. [Inventor]; Lo, Kin-Ming [Inventor]; Qian, Susan X. [Inventor]. Carlisle, MA USA. ASSIGNEE: EMD Lexigen Research Center Corp. Patent Info.: US 07169904 20070130. Official Gazette of the United States Patent and Trademark Office Patents, (JAN 30 2007)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB The invention provides a family of antibodies that specifically bind the human cell surface glycosphingolipid GD2. The antibodies comprise modified variable regions, more specially, modified framework regions, which reduce their immunogenicity when administered to a human. The antibodies may be coupled to a therapeutic agent and used in the treatment of cancer.

L10 ANSWER 2 OF 4 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2006:308336 Document No.: PREV200600313321. Recombinant tumor specific antibody and use thereof. Gillies, Stephen D. [Inventor]; Lo, Kin-Ming [Inventor]; Qian, Susan X. [Inventor]. Carlisle, MA USA. ASSIGNEE: EMD Lexigen Research Center Corp.. Patent Info.: US 06969517 20051129. Official Gazette of the United States Patent and Trademark Office Patents, (NOV 29 2005)
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB The invention provides a family of antibodies that specifically bind the human epithelial cell adhesion molecule. The antibodies comprise modified variable regions, more specially, modified framework regions, which reduce their immunogenicity when administered to a human. The antibodies, when coupled to the appropriate moiety, may be used in the diagnosis, prognosis and treatment of cancer.

L10 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

2004:534239 Document No. 141:87784 Humanized mouse anti-human GD2 antibody fusion with IL-2 for cancer therapy. Gillies, Stephen D.; Lo, Kin-ming (Merck Patent GmbH, Germany). PCT Int. Appl. WO 2004055056 A1 20040701, 51 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-EP14295 20031216. PRIORITY: US 2002-433945P 20021217.

AB The invention provides humanized mouse antibody 14.18 binding the human cell surface glycosphingolipid GD2. The antibody comprises modified variable regions, more specially, modified framework regions, which reduce their immunogenicity when administered to a human. The antibody may be coupled to the therapeutic agent such as IL-2 and used in the treatment of cancer.

L10 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2007 ACS on STN

2002:869105 Document No. 137:368582 Chimeric proteins comprising antibody specific to human epithelial cell adhesion molecule and cytokine for cancer diagnosis, prognosis and therapy. Gillies, Stephen D.; Lo, Kin-Ming; Qian, Xiuqi (Lexigen Pharmaceuticals Corp., USA). PCT Int. Appl. WO 2002090566 A2 20021114, 82 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US13844 20020503. PRIORITY: US 2001-288564P 20010503.

AB The invention provides a family of antibodies that specifically bind the human epithelial cell adhesion mol. The antibodies comprise modified variable regions, more specially, modified framework regions, which reduce their immunogenicity when administered to a human. The antibodies, when coupled to the appropriate moiety, may be used in the diagnosis, prognosis and treatment of cancer.

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=> s l8 and aligning
L11        214 L8 AND ALIGNING

=> s l11 and hypervariable region
L12          5 L11 AND HYPERVARIABLE REGION

=> s l12 and consensus sequence
L13          5 L12 AND CONSENSUS SEQUENCE

=> s l13 and framework residues
L14          0 L13 AND FRAMEWORK RESIDUES

=> dup remove l13
PROCESSING COMPLETED FOR L13
L15           1 DUP REMOVE L13 (4 DUPLICATES REMOVED)

=> d l15 cbib abs
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L15 ANSWER 1 OF 1 MEDLINE on STN DUPLICATE 1
1998308025. PubMed ID: 9642095. Automated classification of antibody complementarity determining region 3 of the heavy chain (H3) loops into canonical forms and its application to protein structure prediction. Oliva B; Bates P A; Querol E; Aviles F X; Sternberg M J. (Universitat Autonoma de Barcelona, 08193 Bellaterra, Barcelona, Spain.) Journal of molecular biology, (1998 Jun 26) Vol. 279, No. 5, pp. 1193-210. Journal code: 2985088R. ISSN: 0022-2836. Pub. country: ENGLAND: United Kingdom. Language: English.

AB A computer-based algorithm was used to cluster the loops forming the complementarity determining region (CDR) 3 of the heavy chain (H3) into canonical classes. Previous analyses of the three-dimensional structures of CDR loops (also known as the hypervariable regions) within antibody immunoglobulin variable domains have shown that for five of the six CDRs there are only a few main-chain conformations (known as canonical forms) that show clear relationships between sequence and structure. However, the larger variation in length and conformation of loops within H3 has limited the classification of these loops into canonical forms. The clustering procedure presented here is based on aligning the Ramachandran-coded main-chain conformation of the residues using a dynamic algorithm that allows the insertion of gaps to obtain an optimum alignment. A total of 41 H3 loops out of 62 non-identical loops, extracted from the Brookhaven Protein Data Bank, have been automatically grouped into 22 clusters. Inspection of the clusters for consensus sequences or intra-loop interactions or invariant conformation led to the proposal of 13 canonical forms representing 31 loops. These canonical forms include a consideration of the geometry of both the take-off region adjacent to the bracing beta-strands and the remaining loop apex. Subsequently a new set of 15 H3 loops not included in the initial analysis was considered. The clustering procedure was repeated and nine of these 15 loops could be assigned to original clusters, including seven to canonical forms. A sequence profile was generated for each canonical form from the original set of loops and matched against the sequences of the new H3 loops. For five out of the seven new H3 loops that were in a canonical form, the correct form was identified at first rank by this predictive scheme.
Copyright 1998 Academic Press.

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(FILE 'HOME' ENTERED AT 11:47:08 ON 20 AUG 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 11:47:26 ON 20 AUG 2007

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L1        71694 S ANTIBODY PRODUCTION
L2          101 S L1 AND HIGH YIELD
L3            0 S L2 AND FRAMEWORK MODIFICATION
L4           12 S L2 AND MODIFIED
L5            0 S L4 AND FRAMEWORK
L6            6 DUP REMOVE L4 (6 DUPLICATES REMOVED)
L7            0 S L1 AND MODIFIED FRAMEWORK
L8      3011979 S ANTIBOD?
L9            4 S L8 AND MODIFIED FRAMEWORK
L10           4 DUP REMOVE L9 (0 DUPLICATES REMOVED)
L11         214 S L8 AND ALIGNING
L12           5 S L11 AND HYPERVARIABLE REGION
L13           5 S L12 AND CONSENSUS SEQUENCE
L14           0 S L13 AND FRAMEWORK RESIDUES
L15           1 DUP REMOVE L13 (4 DUPLICATES REMOVED)
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Executing the logoff script...

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NEWS 19	JUL 26	USPATFULL/USPAT2 enhanced with IPC reclassification
NEWS 20	JUL 30	USGENE now available on STN
NEWS 21	AUG 06	CAS REGISTRY enhanced with new experimental property tags

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 NEWS 22  AUG 06  BEILSTEIN updated with new compounds
 NEWS 23  AUG 06  FSTA enhanced with new thesaurus edition
 NEWS 24  AUG 13  CA/CAplus enhanced with additional kind codes for granted
                  patents
 NEWS 25  AUG 20  CA/CAplus enhanced with CAS indexing in pre-1907 records
 NEWS 26  AUG 27  Full-text patent databases enhanced with predefined
                  patent family display formats from INPADOCDB
 NEWS 27  AUG 27  USPATOLD now available on STN
 NEWS 28  AUG 28  CAS REGISTRY enhanced with additional experimental
                  spectral property data

 NEWS EXPRESS  29 JUNE 2007:  CURRENT WINDOWS VERSION IS V8.2,
               CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

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=>  file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS                                    SINCE FILE      TOTAL
                                                           ENTRY    SESSION
FULL ESTIMATED COST                                         0.21       0.21

FILE 'MEDLINE' ENTERED AT 12:02:18 ON 30 AUG 2007

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=> s method
L1    16998219 METHOD

=> s l1 and antibod?
L2      668498 L1 AND ANTIBOD?

=> s l2 and improve yield
L3           8 L2 AND IMPROVE YIELD
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=> dup remove l3
PROCESSING COMPLETED FOR L3
L4             6 DUP REMOVE L3 (2 DUPLICATES REMOVED)

=> d l4 1-6 cbib abs

L4   ANSWER 1 OF 6     MEDLINE on STN
2005077340.    PubMed ID: 15607488.   Preparation and in vivo evaluation of
     novel linkers for 211At labeling of proteins. Talanov Vladimir S; Yordanov
     Alexander T; Garmestani Kayhan; Milenic Diane E; Arora Hans C; Plascjak
     Paul S; Eckelman William C; Waldmann Thomas A; Brechbiel Martin W.
     (Radiation Oncology Branch, Center for Cancer Research, National Cancer
     Institute, National Institutes of Health, Bethesda, MD 20892, USA. )
     Nuclear medicine and biology, (2004 Nov) Vol. 31, No. 8, pp. 1061-71.
     Journal code: 9304420. ISSN: 0969-8051. Pub. country: England: United
     Kingdom. Language: English.
AB   The syntheses, radiolabeling, antibody conjugation and in vivo
     evaluation of new linkers for (211)At labeling of monoclonal
     antibodies are described.  Syntheses of the N-succinimidyl esters
     and labeling with (211)At to form succinimidyl 4-methoxymethyl-3-
     [(211)At]astatobenzoate (9) and succinimidyl 4-methylthiomethyl-3-
     [(211)At]astatobenzoate (11) from the corresponding bromo-aryl esters is
     reported.  Previously reported succinimidyl N-{4-
     [(211)At]astatophenethyl}succinamate (SAPS) is employed as a standard of
     in vivo stability.  Each agent is conjugated with Herceptin in parallel
     with their respective (125)I analogue, succinimidyl 4-methoxymethyl-3-
     [(125)I]iodobenzoate (10), succinimidyl 4-methylthiomethyl-3-
     [(125)I]iodobenzoate (12) and succinimidyl N-{4-
     [(125)I]iodophenethyl}succinamate (SIPS), respectively, for comparative
     assessment in LS-174T xenograft-bearing mice.  With 9 and 11, inclusion of
     an electron pair donor in the ortho position does not appear to provide in
     vivo stability comparable to SAPS.  Variables in radiolabeling chemistry
     of these three agents with (211)At are notable.  Sequential elimination of
     acetic acid and oxidizing agent, N-chlorosuccinimide (NCS), from the
     (211)At radiolabeling protocol for forming SAPS improves
     yield, product purity and consistency.  NCS appears to be critical
     for the radiolabeling of 6 with (211)Atomic  Formation of 11, however, is
     found to require the absence of NCS.  Elimination of acetic acid is found
     to have no effect on radiolabeling efficiency or yield for either of these
     reactions.

L4   ANSWER 2 OF 6  SCISEARCH  COPYRIGHT (c) 2007 The Thomson Corporation  on
     STN
2004:386546   The Genuine Article (R) Number: BY84D. A review of the food/feed
     safety and benefits of Bacillus thuringiensis protein containing
     insect-protected crops.  Hammond B (Reprint). Monsanto Co, Prod Safety
     Ctr, 800 N Lindbergh Blvd, St Louis, MO 63167 USA (Reprint); Monsanto Co,
     Prod Safety Ctr, St Louis, MO 63167 USA. AGRICULTURAL BIOTECHNOLOGY:
     CHALLENGES AND PROSPECTS (2004) Vol. 866, pp. 103-123. ISSN: 0097-6156.
     Publisher: AMER CHEMICAL SOC, 1155 SIXTEENTH ST NW, WASHINGTON, DC 20036
     USA. Language: English.
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB        Infestation of agricultural crops by insect pests has been
     traditionally managed through the use of chemical insecticides.  An
     alternative method to control insect pests has been the
     introduction of insecticidal proteins from Bacillus thuringiensis into
     agricultural crops by genetic engineering.  The introduced insect control
     proteins have an exemplary safety record having been safely used in
     agriculture for 40 years as the active ingredients of microbial
     pesticides.  Insect-protected biotech crops control a variety of insect
     pests such as corn borers, cotton bollworms, and Colorado potato beetles.
     Season long protection of the crop improves yield and
```

reduces reliance on traditional chemical insecticides. Protection of corn plants against insect damage reduces infection by certain fungal pathogens that produce fumonisin mycotoxins that are toxic to various species.

L4 ANSWER 3 OF 6 MEDLINE on STN DUPLICATE 1
2003435074. PubMed ID: 13129388. Improved yield and stability of L49-sFv-beta-lactamase, a single-chain antibody fusion protein for anticancer prodrug activation, by protein engineering. McDonagh Charlotte F; Beam Kevin S; Wu Gabrielle J S; Chen Judy H; Chace Dana F; Senter Peter D; Francisco Joseph A. (Seattle Genetics Inc, 21823 30th Drive SE, Bothell, Washington 98021, USA.. cmcdonagh@seagen.com) . Bioconjugate chemistry, (2003 Sep-Oct) Vol. 14, No. 5, pp. 860-9. Journal code: 9010319. ISSN: 1043-1802. Pub. country: United States. Language: English.
AB The L49 single-chain Fv fused to beta-lactamase (L49-sFv-bL) combined with the prodrug C-Mel is an effective anticancer agent against tumor cells expressing the p97 antigen. However, large-scale production of L49-sFv-bL from refolded E. coli inclusion bodies has been problematic due to inefficient refolding and instability of the fusion protein. Sequence analysis of the L49-sFv framework regions revealed three residues in the framework regions at positions L2, H82B, and H91, which are not conserved for their position, occurring in <1% of sequences in Fv sequence databases. One further unusual residue, found in <3% of variable sequences, was observed at position H39. Each unusual residue was mutated to a conserved residue for its position and tested for refolding yield from inclusion bodies following expression in E. coli. The three V(H) single mutants showed improvement in the yield of active protein and were combined to form double and triple mutants resulting in a 7-8-fold increased yield compared to the parental protein. In an attempt to further improve yield, the orientation of the triple mutant was reversed to create a bL-L49-sFv fusion protein resulting in a 3-fold increase in expressed inclusion body protein and producing a 20-fold increase in the yield of purified protein compared to the parental protein. The triple mutants in both orientations displayed increased stability in murine plasma and binding affinity was not affected by the introduced mutations. Both triple mutants also displayed potent in vitro cytotoxicity and in vivo antitumor activity against p97 expressing melanoma cells and tumor xenografts, respectively. These results show that a rational protein-engineering approach improved the yield, stability, and refolding characteristics of L49-sFv-bL while maintaining binding affinity and therapeutic efficacy.

L4 ANSWER 4 OF 6 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
2001362150 EMBASE Yield of large-volume blood cultures in patients with early lyme disease. Wormser G.P.; Bittker S.; Cooper D.; Nowakowski J.; Nadelman R.B.; Pavia C.. Dr. G.P. Wormser, Div. of Infectious Diseases, Macy Pavilion, Westchester Medical Center, New York, NY 10595, United States. Journal of Infectious Diseases Vol. 184, No. 8, pp. 1070-1072 15 Oct 2001.
Refs: 12.
ISSN: 0022-1899. CODEN: JIDIAQ
Pub. Country: United States. Language: English. Summary Language: English.
Entered STN: 20011025. Last Updated on STN: 20011025
AB To improve yield, 6 3-mL plasma cultures (18 mL total) were established for adult patients with early Lyme disease associated with erythema migrans. Borrelia burgdorferi was recovered from the blood of 22 (44.0%) of 50 evaluable patients. The recovery rate per plasma culture and the frequency of positive results for plasma cultures for individual patients were consistent with a level of spirochetemia of .apprx.0.1 cultivable cell/mL of whole blood. Our findings suggest that, if further improvements in the yield of blood cultures are possible, they

probably will depend on enhancing the sensitivity of the culture method rather than increasing the volume of material cultured.

L4 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2007 ACS on STN
2000:774014 Document No. 133:330525 Process for producing natural folded eukaryotic proteins with prokaryotes. (F. Hoffmann-La Roche A.-G., Switz.). Eur. Pat. Appl. EP 1048732 A1 20001102, 40 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (German). CODEN: EPXXDW. APPLICATION: EP 1999-107412 19990426.

AB The title process for producing eukaryotic proteins, especially disulfide bond-containing eukaryotic proteins, comprises creation of a chimeric gene consisting of a prokaryotic signal sequence fused to a gene for the desired protein, expression of the gene in the prokaryote, and removal of the signal peptide and isolation of the protein from the periplasm or culture medium. The culture contains arginine or R2CONRR1 (R,R1 = H, (unsatd.,branched)C1-4-alkyl; R2 = H, NHR1, (unsatd.,branched)C1-3-alkyl). The culture medium may addnl. contain a reducing agent such as glutathione. To further improve yields, mol. chaperones such as DnaJ or HSP25 may be coexpressed. Thus, E. coli coexpressing a pelB signal sequence-plasminogen activator chimeric gene and a dnaJ gene was cultured in a medium containing glutathione and arginine hydrochloride. The yield of the plasminogen activator was increased approx. 100-fold by this method. A similar method was used to produced an anti-TSH scFv.

L4 ANSWER 6 OF 6 MEDLINE on STN DUPLICATE 2
95375258. PubMed ID: 7647323. Comparison of four methods to generate immunoreactive fragments of a murine monoclonal antibody OC859 against human ovarian epithelial cancer antigen. Zou Y; Bian M; Yiang Z; Lian L; Liu W; Xu X. (Department of Obstetrics and Gynecology, PUMC Hospital, Beijing.) Chinese medical sciences journal = Chung-kuo i hsueh k'o hsueh tsa chih / Chinese Academy of Medical Sciences, (1995 Jun) Vol. 10, No. 2, pp. 78-81. Journal code: 9112559. ISSN: 1001-9294. Pub. country: China. Language: English.

AB In the present study, four different proteases (pepsin, papain, bromelain and ficin) were screened with a murine monoclonal antibody OC859, in order to verify whether different digestion procedures could improve yield and stability of the F(ab')2 or Fab fragments. The yields of F(ab')2 or Fab fragments from digestion with pepsin, papain, bromelain and ficin were respectively 20.3 +/- 2.0%, 50.5 +/- 5.0%, 74.4 +/- 2.7% and 82.8 +/- 10.2% of the theoretical maximum. Immunoreactivity in a noncompetitive solid-phase radioimmunoassay (SPRIA) of the fragments generated by the four proteases were respectively 10 +/- 5%, 36 +/- 5%, 60 +/- 6% and 75 +/- 6% of the intact OC859 IgG. These results suggested that the fragmentation of OC859 with ficin gave a higher yield of superior immunoreactive fragments.

=> s l2 and recombinant
L5 53587 L2 AND RECOMBINANT

=> s l5 and high yield
L6 221 L5 AND HIGH YIELD

=> s l6 and framework substitution
L7 0 L6 AND FRAMEWORK SUBSTITUTION

=> s l6 and substitution
L8 3 L6 AND SUBSTITUTION

=> dup remove l8

PROCESSING COMPLETED FOR L8
L9 3 DUP REMOVE L8 (0 DUPLICATES REMOVED)

=> d l9 1-3 cbib abs

L9 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN
2002:69451 Document No. 136:129931 Construction of recombinant influenza viruses with bicistronic viral RNAs encoding two tandemly arranged genes and uses for vaccination. Hobom, Gerd; Menke, Anette; Meyer-Rogge, Sabine (Artemis Pharmaceuticals G.m.b.H., Germany). Eur. Pat. Appl. EP 1174514 A1 20020123, 39 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2000-115626 20000720.
AB The invention provides recombinant influenza viruses for high-yield expression of incorporated foreign gene(s), which are genetically stable in the absence of any helper virus and comprise at least one viral RNA segment being a tandem bicistronic RNA mol. coding for two genes in tandem arrangement. In particular, one of the standard viral genes in the tandem is in covalent junction with a foreign, recombinant gene and having an upstream splice donor and a downstream splice acceptor signal surrounding the proximal coding region. The invention further provides a method for obtaining attenuated viruses which resist reassortment dependent progeny production in case of superinfections by wild-type influenza viruses. The invention also provides a method for the production of the recombinant influenza viruses, pharmaceutical compns. comprising the recombinant influenza viruses, and use of the recombinant influenza viruses for preparing medicaments for vaccination purposes, immunotherapy and gene therapy.

L9 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
1999:443729 Document No.: PREV199900443729. Distinct immunological and biochemical properties of thyroid peroxidase purified from human thyroid glands and recombinant protein produced in insect cells. Gardas, Andrej; Sutton, Brian J.; Piotrowska, Urszula; Pasieka, Zbigniew; Barnett, Phillip S.; Huang, GuoCai; McGregor, Alan M.; Banga, J. Paul [Reprint author]. Department of Medicine, King's College School of Medicine, Bessemer Road, London, SE5 9PJ, UK. Biochimica et Biophysica Acta, (Aug. 17, 1999) Vol. 1433, No. 1-2, pp. 229-239. print.
CODEN: BBACAQ. ISSN: 0006-3002. Language: English.
AB The biosynthesis of thyroid hormone from thyroglobulin is catalysed by thyroid peroxidase (TPO), an integral membrane protein. TPO is also a major autoantigen in autoimmune thyroid disease and autoantibodies to TPO are markers for disease activity. Large quantities of purified TPO are essential for elucidating its structure and understanding its role in disease activity. We describe the high yield purification of full-length recombinant human TPO from baculovirus infected insect cells and compare it to purified native TPO from human thyroid glands. In contrast to native human TPO, the human TPO produced in insect cells as a recombinant protein was insoluble and resistant to solubilisation in detergents. Reversible substitution of lysine residues with citraconic anhydride led to increased solubility of the recombinant TPO, allowing high-yield purification by monoclonal antibody chromatography. The purified enzyme preparation was shown to be TPO by its reactivity with monoclonal and polyclonal antibodies by enzyme linked immunosorbent assay and Western blotting. Both the human and recombinant purified TPO preparations also react with sera from patients with autoimmune thyroid disease, although the binding of conformational dependent autoantibodies was considerably lower to the recombinant TPO than to the native TPO. This suggests that the recombinant TPO may differ in some aspects of its tertiary

structure. The purified recombinant TPO was devoid of enzyme activity, in contrast to the enzymatically active, purified human TPO preparations. Both preparations contained comparable amounts of haem (Rz = 0.269), but a shift in the Soret band of recombinant TPO (402 nm) from that of natural TPO (409 nm) indicates that the lack of enzymatic activity of the recombinant enzyme may be due to changes in the protein backbone surrounding the haem. Both the purified native and recombinant TPO, under non-denaturing conditions, show evidence of high molecular mass oligomers, althoughthe latter preparation is prone to a greater degree of aggregation. In conclusion, our studies indicate that recombinant TPO generated in insect cells is conformationally distinct from the native TPO, is insoluble and enzymatically inactive, consistent with the difficulties associated with its purification and crystallisation.

L9 ANSWER 3 OF 3 MEDLINE on STN
1999285282. PubMed ID: 10356794. Co-operative effects of protein engineering and vector optimization on high yield expression of functional bivalent miniantibodies in Escherichia coli. Kujau M J; Riesenberg D. (Hans-Knoll-Institut fur Naturstoff-Forschung Jena, Dept. Applied Microbiology, Germany.. mkujau@pmail.hki-jena.de) . Microbiological research, (1999 May) Vol. 154, No. 1, pp. 27-34. Journal code: 9437794. ISSN: 0944-5013. Pub. country: GERMANY: Germany, Federal Republic of. Language: English.
AB The volumetric yield of functional phosphocholine-binding miniantibodies could be increased in E. coli fermentations by the combination of the following approaches: Firstly, miniantibody mutants with amino acid exchanges in the VH chain leading to improved folding were expressed. Secondly, the expression vector was stabilized by an efficient suicide system to prevent plasmid loss. Thirdly, the cells were grown to high cell densities in a stirred tank reactor.

=> s l5 and hypervariable region
L10 64 L5 AND HYPERVARIABLE REGION

=> s l10 and substitution
L11 6 L10 AND SUBSTITUTION

=> dup remove l11
PROCESSING COMPLETED FOR L11
L12 2 DUP REMOVE L11 (4 DUPLICATES REMOVED)

=> d l12 1-2 cbib abs

L12 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
1998:388614 Document No. 129:66834 Mutant species-dependent antibodies and methods for their preparation. Jardieu, Paula M.; Presta, Leonard G. (Genentech, Inc., USA). PCT Int. Appl. WO 9823746 A1 19980604, 72 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1997-US20169 19971029. PRIORITY: US 1996-756150 19961127.
AB Mutants of species-dependent antibodies are disclosed which have at least one amino acid substitution in a hypervariable region and a binding affinity for an antigen from a nonhuman mammal which is at least about 10-fold greater than the binding affinity

of the species-dependent antibody for the antigen.
Methods for prepared such mutants with recombinant cells
are disclosed. Thus, the humanization and in vitro biol. efficacy of
murine anti-human CD11a monoclonal antibody MHM23 is described.
Both the murine and humanized MAbs effectively prevented adhesion of human
T cells to human keratinocytes and the proliferation of T cells in
response to nonautologous leukocytes in the mixed lymphocytes response.
However, both MAbs did not cross-react with nonhuman primate CD11a other
than chimpanzee CD11a. In order to have a humanized MAb available for
preclin. studies in rhesus monkey, the humanized MAb was re-engineered to
bind to rhesus CD11a by changing 4 residues in one of the
complementarity-determining regions in the variable heavy domain. Cloning and
mol. modeling of the rhesus CD11a I-domain suggested that a change from a
Lys in human CD11a I-domain to Glu in rhesus CD11a I-domain is the reason
that the murine and humanized MAbs did not bind rhesus CD11a.

L12 ANSWER 2 OF 2 MEDLINE on STN DUPLICATE 1
1998085910. PubMed ID: 9425941. Comparison of the rate of sequence
variation in the hypervariable region of E2/NS1 region
of hepatitis C virus in normal and hypogammaglobulinemic patients. Booth J
C; Kumar U; Webster D; Monjardino J; Thomas H C. (Academic Department of
Medicine, St. Mary's Hospital Medical School, Imperial College of Science,
Technology and Medicine, London, England, UK.) Hepatology (Baltimore,
Md.), (1998 Jan) Vol. 27, No. 1, pp. 223-7. Journal code: 8302946. ISSN:
0270-9139. Pub. country: United States. Language: English.
AB The hypervariable region (HVR) of the E2/NS1 region of
hepatitis C virus (HCV) varies greatly between viral isolates with high
rates of genomic change reported during the course of chronic infection.
The HVR is thought to encode a structurally unconstrained envelope protein
containing several linear B cell epitopes recognized by neutralizing
antibody. It has been postulated that amino acid changes in the
HVR could result from humoral immune pressure leading to the selection of
escape mutants. The aim of this study was to compare the rates of
nucleotide and amino acid variation in the HVR of control patients to
patients with common variable immunodeficiency (CVID) where the effect of
the humoral immune system is reduced. Five controls and four patients
with CVID were studied. Serum samples were taken over periods of between
1 and 6 years. HCV was detected by polymerase chain reaction (PCR) with
primers derived from conserved flanking regions of the HVR. PCR products
were cloned into a plasmid vector and recombinant clones
identified by restriction enzyme digestion. Purified DNA from at least
three individual clones from each time point was sequenced by the
dideoxynucleotide chain-termination method. Consensus sequences
were extracted from the three clones, and the DNA and deduced protein
sequences were compared. Control patients had a mean rate of nucleotide
change of 6.954 nucleotide substitutions per year, compared with
patients with CVID with a rate of 0.415 nucleotide substitutions
per year ($P < .02$). The corresponding rates for amino acid variation were
3.868 amino acid substitutions per year for the control patients
compared with 0.185 amino acid substitutions per year for the
patients with CVID. These findings suggest that in the absence of humoral
immune selective pressure, the frequency of occurrence of genetic
variation in the major viral species is reduced. The mutations occur, but
in the absence of immune selection remain as minor species. The evolution
of viral mutants capable of evading the host's immune system may
contribute to the ability of HCV to establish chronic infection.

=> d his

(FILE 'HOME' ENTERED AT 12:02:01 ON 30 AUG 2007)

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     FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 12:02:18 ON
     30 AUG 2007
L1     16998219 S METHOD
L2       668498 S L1 AND ANTIBOD?
L3            8 S L2 AND IMPROVE YIELD
L4            6 DUP REMOVE L3 (2 DUPLICATES REMOVED)
L5        53587 S L2 AND RECOMBINANT
L6          221 S L5 AND HIGH YIELD
L7            0 S L6 AND FRAMEWORK SUBSTITUTION
L8            3 S L6 AND SUBSTITUTION
L9            3 DUP REMOVE L8 (0 DUPLICATES REMOVED)
L10          64 S L5 AND HYPERVARIABLE REGION
L11           6 S L10 AND SUBSTITUTION
L12           2 DUP REMOVE L11 (4 DUPLICATES REMOVED)

=> s l2 and amino acid substitution
L13       1187 L2 AND AMINO ACID SUBSTITUTION

=> s l13 and modified framework
L14          0 L13 AND MODIFIED FRAMEWORK

=> s l13 and consensus sequence
L15         21 L13 AND CONSENSUS SEQUENCE

=> dup remove l15
PROCESSING COMPLETED FOR L15
L16          16 DUP REMOVE L15 (5 DUPLICATES REMOVED)

=> d l16 1-16 cbib abs

L16  ANSWER 1 OF 16     MEDLINE on STN
2006211427.    PubMed ID: 16307801.   A novel small reporter gene and HIV-1
     fitness assay. Ali Ayub; Yang Otto O. (Division of Infectious Diseases,
     Department of Medicine, UCLA Medical Center, David Geffen School of
     Medicine at UCLA, Los Angeles, CA 90095, USA. ) Journal of virological
     methods, (2006 Apr) Vol. 133, No. 1, pp. 41-7.  Electronic Publication:
     2005-11-22. Journal code: 8005839. ISSN: 0166-0934. Pub. country:
     Netherlands. Language: English.
AB   Most currently available HIV-1 reporter gene constructs are large and
     disrupt the nef reading frame.  This report describes a novel reporter
     gene based on the small murine heat stable antigen (HSA) protein, which is
     expressed on the surface of infected cells.  This HSA reporter can be
     inserted in the vpr reading frame, leaving nef intact.  Nine amino acids
     from the extracellular domain of HSA are replaced with an influenza
     hemagglutinin (HA) antibody epitope (HSA-HA).  Like the parental
     reporter protein, this novel reporter is expressed on the surface of
     infected cells.  Antibodies for HSA and HA specifically detect
     reporter viruses with each construct, indicating disruption of the
     original HSA antibody epitope.  Finally, a strategy is developed
     to detect each reporter virus by real-time PCR quantitation.  The growth
     of viruses tagged with each reporter allows precise assessment of the
     relative growth of viruses differing in mutations of interest.  Moreover,
     the availability of these reporters in either of two half-genome plasmids
     allows convenient production of reporter and non-reporter HIV-1 by
     co-transfection of appropriately paired plasmids.  These paired reporter
     viruses offer a potentially useful standardized method for
     measurement of HIV-1 fitness in competition assays.

L16  ANSWER 2 OF 16  SCISEARCH  COPYRIGHT (c) 2007 The Thomson Corporation  on
     STN
2005:12991   The Genuine Article (R) Number: 879IG. Synthetic peptide vaccine
     development: measurement of polyclonal antibody affinity and
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cross-reactivity using a new peptide capture and release system for surface plasmon resonance spectroscopy. Cachia P J; Kao D J; Hodges R S (Reprint). Univ Colorado, Hlth Sci Ctr, Dept Biochem & Mol Genet, Biomed Res Bldg, Rm 451 BRB, 4200 E 9th Ave, B-121, Denver, CO 80262 USA (Reprint); Univ Colorado, Hlth Sci Ctr, Dept Biochem & Mol Genet, Denver, CO 80262 USA. robert.hodges@uchsc.edu. JOURNAL OF MOLECULAR RECOGNITION (NOV-DEC 2004) Vol. 17, No. 6, pp. 540-557. ISSN: 0952-3499. Publisher: JOHN WILEY & SONS LTD, THE ATRIUM, SOUTHERN GATE, CHICHESTER PO19 8SQ, W SUSSEX, ENGLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB A method has been developed for measurement of antibody affinity and cross-reactivity by surface plasmon resonance spectroscopy using the EK-coil heterodimeric coiled-coil peptide capture system. This system allows for reversible capture of synthetic peptide ligands on a biosensor chip surface, with the advantage that multiple antibody-antigen interactions can be analyzed using a single biosensor chip. This method has proven useful in the development of a synthetic peptide anti-Pseudomonas aeruginosa (PA) vaccine. Synthetic peptide ligands corresponding to the receptor binding domains of pilin from four strains of PA were conjugated to the E-coil strand of the heterodimeric coiled-coil domain and individually captured on the biosensor chip through dimerization with the immobilized K-coil strand. Polyclonal rabbit IgG raised against pilin epitopes was injected over the sensor chip surface for kinetic analysis of the antigen-anti body interaction. The kinetic rate constants, k(on) and k(off), and equilibrium association and dissociation constants, KA and KD, were calculated. Antibody affinities ranged from 1.14 x 10(-9) to 1.60 x 10(-5) M. The results suggest that the carrier protein and adjuvant used during immunization make a dramatic difference in antibody affinity and cross-reactivity. Antibodies raised against the PA strain K pilin epitope conjugated to keyhole limpet haemocyanin using Freund's adjuvant system were more broadly cross-reactive than antibodies raised against the same epitope conjugated to tetanus toxoid using Adjuvax adjuvant. The method described here is useful for detailed characterization of the interaction of polyclonal antibodies with a panel of synthetic peptide ligands with the objective of obtaining high affinity and cross-reactive antibodies in vaccine development. Copyright (C) 2004 John Wiley Sons, Ltd.

L16 ANSWER 3 OF 16 MEDLINE on STN

2003517757. PubMed ID: 14573859. Constraints on the conformation of the cytoplasmic face of dark-adapted and light-excited rhodopsin inferred from antirhodopsin antibody imprints. Bailey Brian W; Mumey Brendan; Hargrave Paul A; Arendt Anatol; Ernst Oliver P; Hofmann Klaus Peter; Callis Patrik R; Burritt James B; Jesaitis Algirdas J; Dratz Edward A. (Department of Chemistry and Biochemistry, Montana State University, Bozeman, Montana 59717-3520, USA.) Protein science : a publication of the Protein Society, (2003 Nov) Vol. 12, No. 11, pp. 2453-75. Journal code: 9211750. ISSN: 0961-8368. Pub. country: United States. Language: English.

AB Rhodopsin is the best-understood member of the large G protein-coupled receptor (GPCR) superfamily. The G-protein amplification cascade is triggered by poorly understood light-induced conformational changes in rhodopsin that are homologous to changes caused by agonists in other GPCRs. We have applied the "antibody imprint" method to light-activated rhodopsin in native membranes by using nine monoclonal antibodies (mAbs) against aqueous faces of rhodopsin. Epitopes recognized by these mAbs were found by selection from random peptide libraries displayed on phage. A new computer algorithm, FINDMAP, was used to map the epitopes to discontinuous segments of rhodopsin that are distant in the primary sequence but are in close spatial proximity in the structure. The proximity of a segment of the N-terminal and the loop

between helices VI and VIII found by FINDMAP is consistent with the X-ray structure of the dark-adapted rhodopsin. Epitopes to the cytoplasmic face segregated into two classes with different predicted spatial proximities of protein segments that correlate with different preferences of the antibodies for stabilizing the metarhodopsin I or metarhodopsin II conformations of light-excited rhodopsin. Epitopes of antibodies that stabilize metarhodopsin II indicate conformational changes from dark-adapted rhodopsin, including rearrangements of the C-terminal tail and altered exposure of the cytoplasmic end of helix VI, a portion of the C-3 loop, and helix VIII. As additional antibodies are subjected to antibody imprinting, this approach should provide increasingly detailed information on the conformation of light-excited rhodopsin and be applicable to structural studies of other challenging protein targets.

L16 ANSWER 4 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2003:458183 Document No.: PREV200300458183. Phosphorylation of the potyvirus capsid protein by protein kinase CK2 and its relevance for virus infection. Ivanov, Konstantin I. [Reprint Author]; Puustinen, Pietri; Gabrenaite, Rasa; Vihinen, Helena; Ronnstrand, Lars; Valmu, Leena; Kalkkinen, Nisse; Makinen, Kristiina [Reprint Author]. Institute of Biotechnology, University of Helsinki, FIN-00014, Helsinki, Finland. konstantin.ivanov@helsinki.fi; kristiina.makinen@helsinki.fi. Plant Cell, (September 2003) Vol. 15, No. 9, pp. 2124-2139. print.
CODEN: PLCEEW. ISSN: 1040-4651. Language: English.
AB We reported previously that the capsid protein (CP) of Potato virus A (PVA) is phosphorylated both in virus-infected plants and in vitro. In this study, an enzyme that phosphorylates PVA CP was identified as the protein kinase CK2. The alpha-catalytic subunit of CK2 (CK2alpha) was purified from tobacco and characterized using in-gel kinase assays and liquid chromatography-tandem mass spectrometry. The tobacco CK2alpha gene was cloned and expressed in bacterial cells. Specific antibodies were raised against the recombinant enzyme and used to demonstrate the colocalization of PVA CP and CK2alpha in infected tobacco protoplasts. A major site of CK2 phosphorylation in PVA CP was identified by a combination of mass spectrometric analysis, radioactive phosphopeptide sequencing, and mutagenesis as Thr-242 within a CK2 consensus sequence. Amino acid substitutions that affect the CK2 consensus sequence in CP were introduced into a full-length infectious cDNA clone of PVA tagged with green fluorescent protein. Analysis of the mutant viruses showed that they were defective in cell-to-cell and long-distance movement. Using in vitro assays, we demonstrated that CK2 phosphorylation inhibited the binding of PVA CP to RNA, suggesting a molecular mechanism of CK2 action. These results suggest that the phosphorylation of PVA CP by CK2 plays an important regulatory role in virus infection.

L16 ANSWER 5 OF 16 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
2003073068 EMBASE The donor splice site mutation in NFκB-inducing kinase of alymphoplasia (aly/aly) mice. Macpherson A.J.; Uhr T.. A.J. Macpherson, Institute of Experimental Immunology, Universitatsspital, Schmelzbergstrasse 12, 8091 Zurich, Switzerland. amacpher@pathol.unizh.ch.
Immunogenetics Vol. 54, No. 10, pp. 693-698 1 Jan 2003.
Refs: 17.
ISSN: 0093-7711. CODEN: IMNGBK
Pub. Country: Germany. Language: English. Summary Language: English.
Entered STN: 20030306. Last Updated on STN: 20030306
AB The alymphoplasia (aly/aly) mouse has a spontaneous mutation maintained on a C57BL/6xAEJ (H-2(b)) background that results in an absence of extrasplenic secondary lymphoid tissues. The cDNA defect has previously been shown to reside in a point mutation causing a G855R substitution in

NFκB-inducing kinase (NIK). Since the aly/aly female cannot lactate, the strain must be bred by intercrossing heterozygous females with homozygous males and the offspring typed by serum IgA levels at the age of 4-6 weeks. We originally determined the genomic location of the alymphoplasia mutation by sequencing boundaries of regions homologous to human NIK exons, although recently the entire genomic sequence of murine C57BL/6 NIK has become available through the mouse genome project. The aly mutation is at position -1 of an intron donor consensus splice site. Exon-connexion PCR confirmed that splicing does occur across this site. Using the genomic information, we also developed a method of PCR typing of aly/aly mice from tail clips, and used this to derive an aly/aly μMT double-mutant strain in which antibody independent typing is essential. Genetic typing should considerably simplify husbandry and manipulation of the aly/aly genetic background, which is widely used as a recipient in lymphocyte transfer experiments to permit examination of the relative role of secondary lymphoid structures in immune responses.

L16 ANSWER 6 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2004:124159 Document No.: PREV200400117073. Serum compartmentalization of hepatits C virus (HCV) quasispecies. Hughes, Michael G. Jr. [Reprint Author]; Chong, Tae W. [Reprint Author]; Smith, Robert L. II [Reprint Author]; Evans, Heather L. [Reprint Author]; Camden, Jeremy R. [Reprint Author]; Sawyer, Robert G. [Reprint Author]; Rudy, Christine K. [Reprint Author]; Pruett, Timothy L. [Reprint Author]. University of Virginia, Charlottesville, VA, USA. Hepatology, (October 2003) Vol. 38, No. 4 Suppl. 1, pp. 473A. print.
Meeting Info.: 54th Annual Meeting of the American Association for the Study of Liver Diseases. Boston, MA, USA. October 24-28, 2003. American Association for the Study of Liver Diseases.
ISSN: 0270-9139 (ISSN print). Language: English.

AB INTRODUCTION: HCV in patient serum has been found in association with low density lipoprotein (LDL) and immunoglobulin G (IgG), in addition to being free. It has never been determined whether the quasispecies of virus in these compartments differs, or just reflects the quasispecies in the serum. Although it is currently unknown which portion of the viral envelope might associate with LDL, the hypervariable region 1 (HVR1) of E2 is known to be bound by IgG. As HVR1 variability has been shown to be driven by immunologic pressure with escape variants generated when IgG is able to associate with the virus, HVR1 quasi-species bound to IgG should differ from those of other serum compartments. HYPOTHESIS: HCV circulates in patient serum as different HVR1 quasispecies populations bound to IgG, LDL or unbound and differs from the quasispecies population of diseased liver. METHODS: In three patients with end stage liver disease secondary to HCV infection, serum samples and liver biopsies were obtained simultaneously. IgG bound HCV was isolated from the unfrozen fraction with protein G beads. Anti-LDL antibody was added to the supernatant and then isolated with protein G beads. HCV in the remaining supernatant was considered unbound virus. The remaining serum was frozen at -80degreeC. RNA was extracted from liver, frozen serum (called total serum) and the IgG, LDL and unbound fractions. RNA was reverse transcribed and then amplified with nested PCR with primers flanking HVR1. PCR product was gel purified and cloned with 15-25 clones directly sequenced to characterized quasispecies variants (as determined by the HVR1 amino acid sequence). RESULTS: Positive strand viral RNA was present in total serum, liver, LDL and unbound fraction for all patients and the IgG fraction for two patients. Multiple quasispecies variants were detected in the serum compartments which were not found in the total serum or liver samples. Consensus sequences were different between all samples for two patients. In one patient, consensus sequences were identical for total serum and unbound fraction as well as for liver and IgG fraction. Though consensus sequences differed, certain variants were found in multiple

samples from the same patient. Genetic complexity (normalized Shannon entropy) was greatest in liver (0.71+-0.11), followed by IgG fraction (0.65+-0.01), LDL fraction (0.60+-0.13), unbound fraction (0.47+-0.40) and total serum (0.40+-0.35). Genetic diversity (percent maximal amino acid divergence as determined by the amino acid substitution matrix BLOSUM62) was more variable: explant (21+-6), IgG fraction (19+-11), LDL fraction (12+-5), unbound fraction (15+-8) and total serum (11+-6). CONCLUSIONS: HVR1 quasispecies populations differ in identity and complexity between serum compartments and liver, however certain variants are able to associate with more than one fraction. It thus appears that there is some specific interaction between LDL and virus, but it is not governed by HVR1.

L16 ANSWER 7 OF 16 MEDLINE on STN
2001147816. PubMed ID: 11139487. Evidence for positive selection in foot-and-mouth disease virus capsid genes from field isolates. Haydon D T; Bastos A D; Knowles N J; Samuel A R. (Centre for Tropical Veterinary Medicine, University of Edinburgh, Roslin, Midlothian, EH25 9RG Scotland.. daniel.haydon@ed.ac.uk) . Genetics, (2001 Jan) Vol. 157, No. 1, pp. 7-15. Journal code: 0374636. ISSN: 0016-6731. Pub. country: United States. Language: English.

AB The nature of selection on capsid genes of foot-and-mouth disease virus (FMDV) was characterized by examining the ratio of nonsynonymous to synonymous substitutions in 11 data sets of sequences obtained from six different serotypes of FMDV. Using a method of analysis that assigns each codon position to one of a number of estimated values of nonsynonymous to synonymous ratio, significant evidence of positive selection was identified in 5 data sets, operating at 1-7% of codon positions. Evidence of positive selection was identified in complete capsid sequences of serotypes A and C and in VP1 sequences of serotypes SAT 1 and 2. Sequences of serotype SAT-2 recovered from a persistently infected African buffalo also revealed evidence for positive selection. Locations of codons under positive selection coincide closely with those of antigenic sites previously identified with the use of monoclonal antibody escape mutants. The vast majority of codons are under mild to strong purifying selection. However, these results suggest that arising antigenic variants benefit from a selective advantage in their interaction with the immune system, either during the course of an infection or in transmission to individuals with previous exposure to antigen. Analysis of amino acid usage at sites under positive selection indicates that this selective advantage can be conferred by amino acid substitutions that share physicochemically similar properties.

L16 ANSWER 8 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2001:322316 Document No.: PREV200100322316. A novel missense mutation in GP Ibbeta prevents the normal maturation and surface expression of the GPIb-IX-V complex in a patient with the Bernard-Soulier syndrome. Strassel, Catherine [Reprint author]; Lanza, Francois [Reprint author]; De La Salle, Corinne [Reprint author]; Baas, Marie-Jeanne [Reprint author]; Cazenave, Jean-Pierre [Reprint author]; Alessi, Marie-Christine; Juhan-Vague, Irene; Pasquet, Jean-Max; Nurden, Paquita; Nurden, Alan T.. U311 INSERM, Etablissement Francais du Sang, Strasbourg, France. Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 816a. print. Meeting Info.: 42nd Annual Meeting of the American Society of Hematology. San Francisco, California, USA. December 01-05, 2000. American Society of Hematology.
CODEN: BLOOAW. ISSN: 0006-4971. Language: English.

AB The Bernard-Soulier syndrome (BSS) is an inherited bleeding disorder characterized by giant platelets and a deficiency or nonfunctioning of the GPIb-IX-V complex. Although many mutations have been described in GPIbalpha, few studies relate to modifications of GPIbbeta in this

syndrome. We now report a novel missense mutation in GPIbbeta in a patient with a severe bleeding syndrome and whose giant platelets showed the morphological and functional abnormalities typical of BSS. Whereas no reactivity was seen with a series of monoclonal antibodies (MoAbs) to the N-terminal domain of GPIbalpha, GPIbbeta and GPIX in Western blotting or flow cytometry, residual positivity was repeatedly seen in flow cytometry with Bx-1 and WM23, MoAbs reacting with the central core region of GPIbalpha, a result confirmed with Triton X-100 permeabilized platelets. Residual GPV was also present. DNA sequencing revealed a homozygous Asn63->Thr mutation in the N-terminal extracellular domain of GPIbbeta and no other abnormalities. More precisely, Asn63 is found at a conserved position within the beta-sheet forming XLXXLXLXXN consensus sequence common to the leucine-rich family. When the mutated GPIbbeta was coexpressed in a stable CHO cell-line with wild-type GPIbalpha and GPIX, flow cytometry, confocal microscopy and immunoprecipitation experiments showed the absence of the GPIb-IX complex at the cell surface. Small amounts of GPIbalpha and GPIbbeta were detected intracellularly, but little GPIX was present. The residual GPIbalpha had a mass of about 70 kDa both in Western blotting and following immunoprecipitation of lysates obtained from metabolically labeled cells. This was close to immature GPIbalpha revealed in CHOalphabetaIX in pulse-chase experiments, suggesting that it was incompletely glycosylated. The 70kDa peptide failed to immunoprecipitate with the mutated (Thr63) GPIbbeta, while confocal microscopy showed the residual GPIbalpha and mutated GPIbbeta to be primarily retained in a preGolgi compartment in the transfected cells. Thus, a single amino acid substitution in the extracellular domain of GPIbbeta can bring about BSS by affecting both GPIX stability and by limiting the maturation of GPIbalpha. GPIbbeta has a key role in regulating GPIb-IX-V biosynthesis.

L16 ANSWER 9 OF 16 MEDLINE on STN DUPLICATE 1

2000122461. PubMed ID: 10655384. Analysis of genetic variability within the immunodominant epitopes of envelope gp41 from human immunodeficiency virus type 1 (HIV-1) group M and its impact on HIV-1 antibody detection. Dorn J; Masciotra S; Yang C; Downing R; Biryahwaho B; Mastro T D; Nkengasong J; Pieniazek D; Rayfield M A; Hu D J; Lal R B. (HIV Immunology and Diagnostics Branch, National Center for HIV, STD and TB Prevention, Centers for Disease Control and Prevntion, Atlanta, Georgia 30333, USA.) Journal of clinical microbiology, (2000 Feb) Vol. 38, No. 2, pp. 773-80. Journal code: 7505564. ISSN: 0095-1137. Pub. country: United States. Language: English.

AB The serodiagnosis of human immunodeficiency virus type 1 (HIV-1) infection primarily relies on the detection of antibodies, most of which are directed against the immunodominant regions (IDR) of HIV-1 structural proteins. Among these, the N-terminal region of gp41 contains cluster I (amino acids [aa] 580 to 623), comprising the cytotoxic T-lymphocyte epitope (AVERYLKDQQLL) and the cysteine loop (CSGKLIC), and cluster II (aa 646 to 682), comprising an ectodomain region (ELDKWA). To delineate the epitope diversity within clusters I and II and to determine whether the diversity affects serologic detection by U.S. Food and Drug Administration (FDA)-licensed enzyme immunoassay (EIA) kits, gp41 Env sequences from 247 seropositive persons infected with HIV-1 group M, subtypes A (n = 42), B (n = 62), B' (n = 13), C (n = 38), D (n = 41), E (n = 18), F (n = 27), and G (n = 6), and 6 HIV-1-infected but persistently seronegative (HIPS) persons were analyzed. While all IDR were highly conserved among both seropositive and HIPS persons, minor amino acid substitutions (<20% for any one residue, mostly conservative) were observed for all subtypes, except for B', in comparison with the consensus sequence for each subtype. Most importantly, none of the observed substitutions among the group M plasma specimens affected antibody detection, since all specimens (n =

152) tested positive with all five FDA-licensed EIA kits. Furthermore, all specimens reacted with a group M consensus gp41 peptide (WGIKQLQARVLAVERYLKDQQLLGIWGCSGKLICTTAVPWNASW), and high degrees of cross-reactivity (>80%) were observed with an HIV-1 group N peptide, an HIV-1 group O peptide, and a peptide derived from the homologous region of gp41 from simian immunodeficiency virus from chimpanzee (SIVcpz). Taken together, these data indicate that the minor substitutions observed within the IDR of gp41 of HIV-1 group M subtypes do not affect antibody recognition and that all HIV-1-seropositive specimens containing the observed substitutions react with the FDA-licensed EIA kits regardless of viral genotype and geographic origin.

L16 ANSWER 10 OF 16 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

1999198435 EMBASE Genetic alterations in the S gene of hepatitis B virus in patients with acute hepatitis B, chronic hepatitis B and hepatitis B liver cirrhosis before and after liver transplantation. Rodriguez-Frias F.; Buti M.; Jardi R.; Vargas V.; Quer J.; Cotrina M.; Martell M.; Esteban R.; Guardia J.. Dr. M. Buti, Liver Unit, Hospital Gen. Univ. Valle Hebron, Paseo Valle Hebron s-n, Barcelona 08035, Spain. Liver Vol. 19, No. 3, pp. 177-182 1999.

Refs: 34.

ISSN: 0106-9543. CODEN: LIVEDR

Pub. Country: Denmark. Language: English. Summary Language: English.

Entered STN: 19990701. Last Updated on STN: 19990701

AB Background: Several studies have shown that hepatitis B immunoglobulin (HBIG) imposes a selection pressure on the hepatitis B virus (HBV) S gene, and that the emergence of mutations in this region would make reinfection after orthotopic liver transplantation (OLT) possible. Aims: This study was undertaken to analyze the presence of HBV S-gene mutations in the different stages of HBV infection and the relationship between HBIG therapy and the emergence of mutations in liver transplant recipients. Methods: The frequency and location of mutations in the coding region of the HBV S gene were studied by PCR and direct sequencing in 30 patients (7 with acute self-limited hepatitis B, 16 with chronic hepatitis B and 7 recipients of (OLT) for HBV-related end stage liver disease who became reinfected). Results: The average number of amino acid changes was higher in patients with a more advanced stage of disease, 0.57 mutations/100 positions in acute hepatitis B and 1.57 in chronic hepatitis B (1.28 in HBeAg-positive and 1.8 in anti-HBe-positive patients). The average number of substitutions in the transplanted patients was 2.7 before OLT and 3 after OLT. No amino acid substitutions were detected in the 'a' determinant of HBsAg in acute hepatitis B, however, 8 substitutions were observed in 6 chronic patients. In 3 OLT patients, 4 substitutions were observed in samples before and after OLT. One of these patients, who had protective levels of anti-HBs, showed 3 additional new amino acid substitutions after OLT, suggesting escape mutant selection by the effect of HBIG therapy. No changes were observed between the consensus sequences obtained several years before and after transplantation, indicating consensus sequence stability. Conclusion: These results show that there is an accumulation of HBV S-gene mutations in HBV-related end-stage liver disease. Prophylaxis with HBIG mainly obtained from acute self-limited hepatitis patients who have a highly homogeneous viral population, may be one factor underlying the reinfection after liver transplantation.

L16 ANSWER 11 OF 16 MEDLINE on STN DUPLICATE 2

1998085910. PubMed ID: 9425941. Comparison of the rate of sequence variation in the hypervariable region of E2/NS1 region of hepatitis C virus in normal and hypogammaglobulinemic patients. Booth J C; Kumar U; Webster D; Monjardino J; Thomas H C. (Academic Department of Medicine, St.

Mary's Hospital Medical School, Imperial College of Science, Technology and Medicine, London, England, UK.) Hepatology (Baltimore, Md.), (1998 Jan) Vol. 27, No. 1, pp. 223-7. Journal code: 8302946. ISSN: 0270-9139. Pub. country: United States. Language: English.

AB The hypervariable region (HVR) of the E2/NS1 region of hepatitis C virus (HCV) varies greatly between viral isolates with high rates of genomic change reported during the course of chronic infection. The HVR is thought to encode a structurally unconstrained envelope protein containing several linear B cell epitopes recognized by neutralizing antibody . It has been postulated that amino acid changes in the HVR could result from humoral immune pressure leading to the selection of escape mutants. The aim of this study was to compare the rates of nucleotide and amino acid variation in the HVR of control patients to patients with common variable immunodeficiency (CVID) where the effect of the humoral immune system is reduced. Five controls and four patients with CVID were studied. Serum samples were taken over periods of between 1 and 6 years. HCV was detected by polymerase chain reaction (PCR) with primers derived from conserved flanking regions of the HVR. PCR products were cloned into a plasmid vector and recombinant clones identified by restriction enzyme digestion. Purified DNA from at least three individual clones from each time point was sequenced by the dideoxynucleotide chain-termination method. Consensus sequences were extracted from the three clones, and the DNA and deduced protein sequences were compared. Control patients had a mean rate of nucleotide change of 6.954 nucleotide substitutions per year, compared with patients with CVID with a rate of 0.415 nucleotide substitutions per year ($P < .02$). The corresponding rates for amino acid variation were 3.868 amino acid substitutions per year for the control patients compared with 0.185 amino acid substitutions per year for the patients with CVID. These findings suggest that in the absence of humoral immune selective pressure, the frequency of occurrence of genetic variation in the major viral species is reduced. The mutations occur, but in the absence of immune selection remain as minor species. The evolution of viral mutants capable of evading the host's immune system may contribute to the ability of HCV to establish chronic infection.

L16 ANSWER 12 OF 16 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

97125367 EMBASE Document No.: 1997125367. No evidence for quasispecies populations during persistence of the coronavirus mouse hepatitis virus JHM: Sequence conservation within the surface glycoprotein gene S in Lewis rats. Stuhler A.; Flory E.; Wege H.; Lassmann H.; Wege H.. H. Wege, Institute of Diagnostic Virology, Fed. Res. Ctr Virus Diseases Animals, Friedrich-Loeffler-lnstitutes, D-17498 Insel Riems, Germany. wege@rie.bfav.de. Journal of General Virology Vol. 78, No. 4, pp. 747-756 1997.
Refs: 53.
ISSN: 0022-1317. CODEN: JGVIAY
Pub. Country: United Kingdom. Language: English. Summary Language: English.
Entered STN: 970529. Last Updated on STN: 970529

AB The surface glycoprotein S (spike) of coronaviruses is believed to be an important determinant of virulence and displays extensive genetic polymorphism in cell culture isolates. This led us to consider whether the observed heterogeneity is reflected by a quasispecies distribution of mutated RNA molecules within the infected organ. Coronavirus infection of rodents is a useful model system for investigating the pathogenesis of virus-induced central nervous system (CNS) disease. Here, we investigated whether genetic changes in the S gene occurred during virus persistence in vivo. We analysed the variability of S gene sequences directly from the brain tissue of Lewis rats infected with the coronavirus mouse hepatitis virus (MHV) variant JHM-Pi using RT-PCR amplification methods.

The S gene sequence displayed a remarkable genetic stability in vivo. No evidence for a quasispecies distribution was found by sequence analysis of amplified S gene fragments derived from the CNS of Lewis rats. Furthermore, the S gene also remained conserved under the selection pressure of a neutralizing antibody. Only a few mutations predicted to result in amino acid changes were detected in single clones. The changes were not represented in the consensus sequence. These results indicate that to retain functional proteins under the constraints of a persistent infection in vivo, conservation of sequence can be more important than heterogeneity.

L16 ANSWER 13 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

1997:180605 Document No.: PREV199799472318. Myosins from angiosperms, ferns, and algae amplification of gene fragments with versatile PCR primers and detection of protein products with a monoclonal antibody to a conserved head epitope. Plazinski, J. [Reprint author]; Elliott, J.; Hurley, U. A.; Burch, J.; Arioli, T.; Williamson, R. E.. Plant Cell Biol. Group, Research Sch. Biol. Sci., Inst. Advanced Studies, Australian Natioanl Univ., GPO Box 475, Canberra, ACT 2601, Australia. Protoplasma, (1997) Vol. 196, No. 1-2, pp. 78-86.
CODEN: PROTA5. ISSN: 0033-183X. Language: English.

AB Myosins providing the motors for the actin-based motility that occurs in diverse plants have proved difficult to study. To facilitate those studies, we describe polymerase chain reaction primers that reliably amplify part of the myosin head from diverse plants, consensus sequences that characterise the amplified product as encoding a class V or class VIII myosin, and a monoclonal antibody that recognises an epitope conserved in the head of most plant, fungal, and animal myosins. A pair of stringent oligonucleotide primers was designed that, when used in the polymerase chain reaction, amplified at least eleven different myosins from five species of angiosperms and one sequence from each of the fern Azolla and the algae Nitella and Phaeodactylum. The amplified products, comprising 126 to 135 nucleotides encoding pan of the myosin head domain, can be used as myosin-specific probes to screen genomic and cDNA libraries. To identify the products of plant myosin genes, we raised a monoclonal antibody (anti-CHE) to a nine amino acid peptide matching a conserved head epitope showing not more than single amino acid substitutions in most published myosin genes. This antibody recognises rabbit skeletal myosin and multiple polypeptides of gt 100 kDa in four angiosperms and in the alga Nitella. Relating the M-r values of immunoreactive bands in Arabidopsis extracts to the predicted M-r values of the products of five myosin genes supports the view that the antibody recognises both myosins V and VIII together with the products of some as yet unsequenced genes. The previously described MB170 antibodies may, in contrast, be specific for one or more type V myosins. Together, the polymerase chain reaction primers and the antibody represent versatile tools for identifying and categorising myosins in diverse plants.

L16 ANSWER 14 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN

1995:485043 Document No.: PREV199598499343. Molecular characterization of two monoclonal antibodies specific for the LDL receptor-binding site of human apolipoprotein E. Raffai, Robert; Maurice, Roger; Weisgraber, Karl; Innerarity, Thomas; Wang, Xingbo; MacKenzie, Roger; Hirama, Tomoko; Watson, David; Rassart, Eric; Milne, Ross [Reprint author]. Lipoprotein Atherosclerosis Group, Dep. Pathol., Univ. Ottawa, Ottawa, ON, Canada. Journal of Lipid Research, (1995) Vol. 36, No. 9, pp. 1905-1918.
CODEN: JLPRAW. ISSN: 0022-2275. Language: English.

AB Apolipoprotein E (apoE), a 299 amino acid protein, is a ligand for the low

density lipoprotein receptor (LDLr). It has been established that basic amino acids situated between apoE residues 136 and 150 participate in the interaction of apoE with the LDLr. Evidence suggests that apoE is heterogeneous on lipoproteins in its conformation and in its ability to react with cell surface receptors. Our goal was to produce mAbs that could serve as conformational probes of the LDLr binding site of apoE. We used a series of apoE variants that have amino acid substitutions at residues 136, 140, 143, 144, 145, 150, 152, and 158 to identify the epitopes of two anti-human apoE monoclonal antibodies (mAbs), 1D7 and 2E8, that inhibit apoE-mediated binding to the LDLr. We show that most of the variants that have reduced reactivity With the LDL receptor also have reduced reactivity with the mAbs. The epitopes for both mAbs appear to include residues 143 through 150 and thus coincide with the LDLr-binding site of apoE. It is notable that mAb 2E8, but not 1D7, resembles the LDLr in showing a reduced reactivity with apoE (Arg-158 fwdarw Cys). While most of the receptor-defective variants involve replacement of apoE residues directly implicated in binding, substitution of Arg-158 by Cys is thought to indirectly affect binding of apoE to the LDLr by altering the conformation of the receptor-binding site. To determine whether the similarity in specificities of the mAbs and the LDLr reflect structural similarities, we cloned and characterized the cDNAs encoding the light and heavy chains of both mAbs. Primary sequence analysis revealed that, although these two antibodies react with overlapping epitopes, their respective complementarity determining regions (CDRs) share little homology, especially those of their heavy chains, The two mAbs, therefore, likely recognize different epitopes or topologies within a limited surface of the apoE molecule. Four negatively charged amino acids were present in the second CDR of the 2E8 heavy chain that could be approximately aligned with acidic amino acids within the consensus sequence of the LDLr ligand-binding domain. This could indicate that mAb 2E8 and the LDLr use a common mode of interaction with apoE.

L16 ANSWER 15 OF 16 MEDLINE on STN

92024075. PubMed ID: 1656585. Naturally occurring mutations within HIV-1 V3 genomic RNA lead to antigenic variation dependent on a single amino acid substitution. Wolfs T F; Zwart G; Bakker M; Valk M; Kuiken C L; Goudsmit J. (Human Retrovirus Laboratory, Academic Medical Centre, Amsterdam, The Netherlands.) Virology, (1991 Nov) Vol. 185, No. 1, pp. 195-205. Journal code: 0110674. ISSN: 0042-6822. Pub. country: United States. Language: English.

AB In a study on the evolution of genomic diversity of HIV-1, genomic RNA was isolated from serum of two individuals. Starting at the time of primary infection we collected six samples of serum from each patient over a period of 5 years. Ninety-four cDNA clones (50 of patient 1 and 44 of patient 495) of part of the envelope coding region including the principal neutralization domain (PND) were sequenced. Around the time of antibody seroconversion, genomic RNA levels reached a peak and the population of sequences was highly homogeneous. In the course of the infection, the number of amino acid substitutions accumulated, which led to a higher genomic diversity within successive samples and a drift in the consensus sequence, progressively differing from the first found consensus sequence. Fixation of a substitution at glycoprotein 120 amino acid 308 was observed in both patients between two time points (patient 1, H----P; patient 495, P----H). With the use of 16-meric synthetic peptides, differing only at the 308 position (H308 versus P308), antibody binding specificity was found to be dependent on this difference. In patient 495, the nonconservative (P308----H) substitution reduced the binding affinity with the patient's antibodies. Furthermore, antibody competition assays showed that the observed substitution at position 308 elicited a new

antibody population, indicating antigenic variation. After the decline of V3-specific antibodies, the simultaneous increase in genomic RNA levels and progression to AIDS in patient 495, a new variant with major changes in the PND emerged, again forming a homogeneous population of sequences.

L16 ANSWER 16 OF 16 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
2002:316911 Document No.: PREV200200316911. Identification of epitopes recognized by monoclonal antibodies directed against HTLV-I envelope surface glycoprotein using peptide phage display. Chagnaud, J. L.; Moynet, D. [Reprint author]; Londos-Gagliardi, D.; Bezian, J. H.; Vincendeau, P.; Fleury, H.; Guillemain, B.. Laboratoire d'Immunologie Moleculaire, Universite Victor Segalen Bordeaux2, 146 rue Leo Saignat, 33076, Bordeaux Cedex, France. daniel.moynet@immol.u-bordeaux2.fr. Letters in Peptide Science, (2001 (2002)) Vol. 8, No. 2, pp. 95-106. print. ISSN: 0929-5666. Language: English.
AB Phage peptide libraries constitute powerful tools for the mapping of epitopes recognized by monoclonal antibodies (mAbs). Using screening of phage displayed random peptide libraries we have characterized the binding epitopes of three mAbs directed against the surface envelope glycoprotein (gp46) of the human T-cell leukemia virus type I (HTLV-I). Two phage libraries, displaying random heptapeptides with or without flanking cysteine residues, were screened for binding to mAbs 7G5D8, DB4 and 4F5F6. The SSSSTPL consensus sequence isolated from constrained heptapeptide library defines the epitope recognized by DB4 mAb and corresponds to the exact region 249-252 of the virus sequence. The APPMLPH consensus sequence isolated from non constrained heptapeptide library defines the epitope recognized by 7G5D8 mAb and corresponds to the region 187-193 with a single amino acid substitution , methionine to leucine at position 190. The third consensus sequence LYWPHD isolated from constrained heptapeptide library defines the epitope recognized by 4F5F6 mAb. It corresponds to an epitope without direct equivalence with the virus sequence. The data presented here showed that 7G5D8 and DB4 mAbs are raised against linear epitopes while 4F5F6 mAb recognized a continuous topographic epitope.

=> s l2 and align?
L17 2227 L2 AND ALIGN?

=> s l17 and hyervariable region
L18 0 L17 AND HYERVARIABLE REGION

=> s l17 and consensus sequence
L19 243 L17 AND CONSENSUS SEQUENCE

=> s l19 and selecting
L20 2 L19 AND SELECTING

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L21 2 DUP REMOVE L20 (0 DUPLICATES REMOVED)

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L21 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN
2004:181064 Document No. 140:216149 Intracellular antibodies.
Cattaneo, Antonio; Maritan, Amos; Visintin, Michela; Rabbitts, Terrence Howard; Settanni, Giovanni (Medical Research Council, UK; SISSA (Scuola Superiore Internazionale di Studi Avanzati)). PCT Int. Appl. WO

2003014960 A2 20030220, 105 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-GB3512 20020801. PRIORITY: GB 2001-19004 20010803; GB 2001-21577 20010906; IT 2001-RM633 20011025; GB 2002-928 20020116; GB 2002-3569 20020214.

AB The authors disclose a method of identifying sequences for intracellular antibodies (ICS) comprising the steps of: (1) creating a database of sequences of validated intracellular antibodies (VIDA database) and aligning the sequences according to Kabat; (2) determining the frequency with which a particular amino acid occurs in each of the positions of the aligned antibodies; (3) selecting a frequency threshold value (LP or consensus threshold) in the range from 70-100 %; (4) identifying the positions of the alignment at which the frequency of a particular amino acid is greater than or equal to the LP value, and (5) identifying the most frequent amino acids in the positions of said alignment.

L21 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2007 ACS on STN

1993:624264 Document No. 119:224264 Methods and materials for preparation of modified antibody variable domains and therapeutic uses thereof. Studnicka, Gary M.; Little, Roger G., II; Fishwild, Dianne M.; Kohn, Fred R. (Xoma Corp., USA). PCT Int. Appl. WO 9311794 A1 19930624, 159 pp. DESIGNATED STATES: W: CA, JP, US; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1992-US10906 19921214. PRIORITY: US 1991-808464 19911213.

AB Methods are described for identifying the amino acid residues of an antibody (Ab) variable domain which may be modified without diminishing the native affinity of the domain for antigen, while reducing its immunogenicity with respect to a heterologous species. Also described are methods for preparing the so-modified Ab variable domains, which are useful for administration to heterologous species, and the Ab variable regions so prepared The methodol. of the invention includes (1) determining the amino acid sequences for light and heavy chain variable regions of the Ab to be modified; (2) aligning by homol. the light chain sequence with a plurality of human light chain sequences, and the heavy chain sequence with a plurality of human heavy chain sequences; (3) identifying amino acids in the light and heavy chain sequences which are least likely to diminish the affinity of the variable region for antigen while, at the same time, reducing its immunogenicity, by selecting each amino acid which is not in an interface region of the Ab variable domain and which is not in a complementarity-determining region or in an antigen-binding region of the Ab variable domain, but which amino acid is in a position exposed to a solvent containing the Ab; and (4) changing each amino acid identified in (3) which aligns with a highly or moderately conserved amino acid in the plurality of human light or heavy chain sequences if the identified amino acid is different from the amino acid in the plurality of human light and heavy chain sequences. The method of the invention was applied to modification of the variable region of murine monoclonal antibody (MAb) H65 (reactive with human CD5 antigen); comparative H65 and human sequences are included, as are sequences of the modified variable regions. Genes encoding humanized H65 light and heavy chain variable regions were constructed, and the humanized H65 Ab was expressed. The low-risk changes made in the course of modification of humanized H65 did not diminish the

binding affinity of this Ab for the CD5 antigen. Also described are depletion of human T-cells from SCID mice by treatment with H65 MAb, the effects of a anti-Lyt-1 MAb (Lyt-1 is the murine equivalent of CD5) on lymphocytes and on collagen-induced arthritis in mice, etc.

=> s antibod?

=> s antibody

=>

---Logging off of STN---

=>
Executing the logoff script...

=> LOG Y

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                 spectral property data

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              AND CURRENT DISCOVER FILE IS DATED 05 JULY 2007.

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                                                       ENTRY    SESSION
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=> s antibod?
L1     3015896 ANTIBOD?

=> s l1 and consensus sequence
L2        5343 L1 AND CONSENSUS SEQUENCE

=> s l2 and improved folding efficiency
L3           0 L2 AND IMPROVED FOLDING EFFICIENCY

=> s l2 and increase yield
L4           0 L2 AND INCREASE YIELD

=> s l1 and substitution
L5       26327 L1 AND SUBSTITUTION

=> s l5 and heavy chain framework
L6           7 L5 AND HEAVY CHAIN FRAMEWORK

=> dup remove l6
PROCESSING COMPLETED FOR L6
L7           3 DUP REMOVE L6 (4 DUPLICATES REMOVED)

=> d l7 1-3 cbib abs
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L7 ANSWER 1 OF 3 CAPLUS COPYRIGHT 2007 ACS on STN

2005:248951 Document No. 142:315233 Modified antibody comprising a substitution mutation which confers increased stability. Krauss, Juergen; Courtenay-Luck, Nigel Stephen; Rybak, Mary (Antisoma PLC, UK; The Government of the United States of America, as Represented by the Secretary of Health and Human Services). Brit. UK Pat. Appl. GB 2406094 A 20050323, 81 pp. (English). CODEN: BAXXDU. APPLICATION: GB 2003-21746 20030917.

AB A modified antibody which selectively binds to a specific target, the antibody being modified at at least one amino acid residue that dets. antigen binding selectivity/affinity characterized in that the antibody mol. exhibits a great stability than the unmodified parent antibody. The mutation may be in the variable heavy domain at position VH71 and comprises the substitution of a smaller amino acid than the native residue. The antibody mol., e.g. a ScFv, diabody, may be derived from a humanized HMFG-1 antibody raised against the cancer specific glycoprotein antigen, MUC-1. Conjugation of the antibody to drugs, toxins, radionuclides, nucleases and the use of the fusion mols. in pharmaceutical compns. for the treatment of cancer, particularly adenocarcinoma, is described. Use of the antibody in a phage display system to identify target mols. is described. Host cells and vectors comprising the nucleic acid of figure 8, encoding the mutated antibody, are also described.

L7 ANSWER 2 OF 3 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

1997:874681 The Genuine Article (R) Number: YH133. Design and construction of a hybrid immunoglobulin domain with properties of both heavy and light chain variable regions. Ill C R (Reprint); Gonzales J N; Houtz E; Ludwig J R; Melcher E D; Hale J E; Pourmand R; Keivens V M; Myers L; Beidler K; Stuart P; Radhakrishnan R. HYBRITECH INC, PROT ENGN GRP, DIV IMAGING & THERAPEUT RES & DEV, SAN DIEGO, CA 92121. PROTEIN ENGINEERING (AUG 1997) Vol. 10, No. 8, pp. 949-957. ISSN: 0269-2139. Publisher: OXFORD UNIV PRESS , GREAT CLARENDON ST, OXFORD, ENGLAND OX2 6DP. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The complementarity-determining regions (CDRs) of a human kappa light chain were replaced with CDRs from a murine gamma-1 heavy chain and, by use of molecular modeling, key heavy chain framework residues were identified and thus included to preserve the native conformation of the heavy chain CDRs, Go-expression of this hybrid human kappa chain (VHBCL) With a human kappa chain counterpart (VLCL, engineered to contain murine light chain CDRs) resulted in the secretion of high levels of a heterodimeric protein (VHBCL::VLCL) termed 'kappabody'. This protein also had equivalent affinity for antigen as the Fab' of the parent murine IgG(1). High-level secretion was also observed for the hybrid chain as homodimers (VHBCL::VHBCL), which is not observed for chimeric chains consisting of a heavy chain variable region and light chain constant region, i.e. VHCL homodimers or single chains are not secreted, This indicates that regions within the variable domain, required for secretion of light chains, reside outside of the hypervariable regions (CDRs) and that the heavy chain CDRs and supporting residues do not prevent secretion, These results demonstrate the possibility of designing small, single-domain molecules possessing a given binding activity which may be secreted at high levels from mammalian cells.

L7 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 1
96062076. PubMed ID: 7473721. Framework residues 71 and 93 of the chimeric B72.3 antibody are major determinants of the conformation of heavy-chain hypervariable loops. Xiang J; Sha Y; Jia Z; Prasad L; Delbaere L T. (Saskatoon Cancer Center, Department of Microbiology, Saskatchewan, Canada.) Journal of molecular biology, (1995 Oct 27) Vol. 253, No. 3, pp. 385-90. Journal code: 2985088R. ISSN: 0022-2836. Pub. country: ENGLAND: United Kingdom. Language: English.
AB Structural analysis derived from the crystallographic study of the chimeric B72.3 antibody illustrated that some heavy-chain framework residues having atomic interactions with heavy-chain CDR residues may directly affect the conformation of CDR loops. For example, an alanine residue at H71 provides room for packing CDR2/CDR1 and lysine residues at H73 and H93 contribute a salt-bridge to aspartic acid at H55 in CDR2 and a hydrogen bond to the carbonyl group at H96 in CDR3, respectively. We have analysed the contribution of these framework residues to the TAG72-binding affinity. We altered these framework residues by site-directed mutagenesis, and determined the affinity of these mutant chimeric antibodies for the TAG72 antigen by solid phase radioimmunoassay. We found that a single amino acid substitution of alanine by phenylalanine at H71 or lysine by isoleucine at H93, significantly reduced the binding affinity for the TAG72 antigen by 12 and 20-fold, respectively, whereas the substitution of lysine by alanine at H73 reduced the binding affinity only two-fold. Our results indicate that heavy-chain framework residues alanine at H71 and lysine at H93 of the chimeric B72.3 antibody are the major determinants of the conformation of heavy-chain CDR2/CDR1 and CDR3 loops, whereas the salt-bridge between lysine at H73 and aspartic acid at H55 is less important. The hydrogen bond between two framework residues, glutamine at H5 and serine at H25 does not affect any CDR conformation. Our results will thus be of importance especially when the humanized B72.3 antibody is constructed by grafting the CDR loops to a human framework. The important framework region interactions must be maintained in the final humanized antibody.

=> s framework consensus sequence
L8 2 FRAMEWORK CONSENSUS SEQUENCE

=> dup remove l8
PROCESSING COMPLETED FOR L8

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L9            2 DUP REMOVE L8 (0 DUPLICATES REMOVED)

=> d l9 1-2 cbib abs

L9   ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
2006:606294   Document No. 145:61466  Humanized anti-human β-amyloid
     peptide antibodies for treating amyloidogenic disease and relevant
     behavioral deficit.  Basi, Gurig; Jacobson, Jack Steven (Neuralab Limited,
     Bermuda; Wyeth, John, and Brother Ltd.).  PCT Int. Appl. WO 2006066049 A2
     20060622, 157 pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA,
     BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,
     EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG,
     KM, KN, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN,
     MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE,
     SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU,
     ZA; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA,
     GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR.
     (English).  CODEN: PIXXD2.  APPLICATION: WO 2005-US45515 20051215.
     PRIORITY: US 2004-636684P 20041215.
AB   The invention provides improved agents and methods for treatment of
     diseases associated with amyloid deposits of Aβ in the brain of a
     patient.  Preferred agents include antibodies, e.g., humanized antibodies.

L9   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
2004:453250   Document No. 141:22210  Single-chain antibodies for intracellular
     targeting of Ras oncoprotein.  Rabbitts, Terence Howard; Tanaka, Tomoyuki
     (Medical Research Council, UK).  PCT Int. Appl. WO 2004046187 A2 20040603,
     67 pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR,
     BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI,
     GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
     LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM,
     PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT,
     TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG,
     CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR,
     NE, NL, PT, SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.  APPLICATION:
     WO 2003-GB4944 20031114.  PRIORITY: GB 2002-26723 20021115.
AB   The authors disclose antibodies which can function in an intracellular
     environment.  In particular, the intracellular antibodies contain
     framework consensus sequences for the heavy
     chain variable region and the light chain variable region which stabilize
     binding to a ligand within an intracellular environment.  In one example,
     the authors demonstrate the inhibition of fibroblast transformation with
     an engineered single-chain antibody targeting a Ras oncoprotein.


=> s increase yield
L10       4363 INCREASE YIELD

=> s l10 and antibod?
L11         32 L10 AND ANTIBOD?

=> dup remove l11
PROCESSING COMPLETED FOR L11
L12          24 DUP REMOVE L11 (8 DUPLICATES REMOVED)

=> d l12 1-24 cbib abs

L12  ANSWER 1 OF 24  CAPLUS  COPYRIGHT 2007 ACS on STN
2007:643891   Document No. 147:65611  Nucleic acid molecules encoding
     polypeptides involved in regulation of sugar and lipid metabolism and
     their use in transgenic plants.  Haertel, Heiko. A.; Bhatt, Garima (Basf
     Plant Science G.m.b.H., Germany).  PCT Int. Appl. WO 2007065878 A2
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20070614, 129pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2006-EP69271 20061204. PRIORITY: US 2005-597558P 20051209.

AB This invention relates generally to nucleic acid sequences encoding proteins that are related to the presence of seed storage compds. in plants. More specifically, the present invention relates to Arabidopsis thaliana, Brassica napus, Glycine max, and Oryza sativa nucleic acid sequences encoding sugar and lipid metabolism regulator proteins and the use of these sequences in transgenic plants. In particular, the invention is directed to methods for manipulating sugar-related compds. and for increasing oil level and altering the fatty acid composition in plants and seeds. The invention further relates to methods of using these novel plant polypeptides to stimulate plant growth and/or to increase yield and/or composition of seed storage compds.

L12 ANSWER 2 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN

2007:538620 Document No. 146:516088 Adenoviral protein pIX as a productivity augmenting protein factor in novel cell lines for recombinant protein production. Sandig, Volker; Jordan, Ingo (Probiogen AG, Germany). PCT Int. Appl. WO 2007054516 A1 20070518, 56pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2006-EP68234 20061108. PRIORITY: EP 2005-110453 20051108; US 2005-750156P 20051214.

AB The present invention provides a method for preparing a non-adenoviral target virus or target proteins utilizing a potent expression cell line having stably integrated into its genome a gene encoding a specific heterologous regulator protein. Because of its known pleotropic effects, the adenoviral pIX protein was transfected into cell lines to exam. whether pIX augments cell proliferation or production properties for biopharmaceutical products that are not related to adenovirus or adenoviral vectors. Unexpectedly, pIX (or a chimeric fusion analog) exerts a phenotypical effect in avian and human cells. Stable presence of pIX increases susceptibility of cell induction by double-stranded RNA analog, probably via Toll-like receptor 3. The presence of pIX protein also increases yields of highly attenuated pox virus in avian host cells, and increases the yield of proteinaceous product (not only virus) released by a stably transfected cell line. NC5T11 and NC5T11puro cell lines were developed from a mixture of cells from fetal brain by immortalization with adenovirus 5 E1A and B genes by nonviral transfection, followed by transfection with the pIX gene or a pIX-retinoic acid receptor fusion protein. Thus, the invention utilizes an expression cell having integrated into its genome a gene encoding adenoviral 5 pIX protein which modulates transcription, influences cell growth, and enhances productivity of the cell line with regard to the production of a virus not containing pIX and/or production of a protein differing from pIX.

L12 ANSWER 3 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN

2006:1356995 Document No. 146:94682 Use of genes for molecular chaperones to

increase yields of proteins manufactured in transgenic expression hosts. Payne, Thomas; Sleep, Darrell; Finnis, Christopher John Arthur; Evans, Leslie Robert (Delta Biotechnology Limited, UK; University of Nottingham). PCT Int. Appl. WO 2006136831 A2 20061228, 302pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LV, LY, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IS, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2006-GB2289 20060622. PRIORITY: GB 2005-12707 20050622.

AB Host cells expressing genes for mol. chaperones and associated helper proteins, such as protein disulfide isomerases and sulfhydryl oxidase are used to stabilize foreign proteins and to increase their yields. The cells express genes for members of the DnaJ family, such a JEM1; and members of the Hsp70 family, such as LHS1 and SIL1 in combinations with genes for helper proteins. The DnaJ-like protein SCJ1 is specifically not used. The genes for these proteins may be expressed from non-native promoters as necessary to increase levels of expression. Use of the method to increase yields of serum albumin and transferrin using a Saccharomyces cerevisiae host is demonstrated.

L12 ANSWER 4 OF 24 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

2006:242891 The Genuine Article (R) Number: 016VC. Versatile and efficient synthesis of protein-polysaccharide conjugate vaccines using aminooxy reagents and oxime chemistry. Lees A (Reprint); Sen G; LopezAcosta A. Biosynexus Inc, 9119 Gaither Rd, Gaithersburg, MD 20877 USA (Reprint); Biosynexus Inc, Gaithersburg, MD 20877 USA; Uniformed Serv Univ Hlth Sci, Bethesda, MD 20814 USA. AndyLees@Biosynexus.com. VACCINE (6 FEB 2006) Vol. 24, No. 6, pp. 716-729. ISSN: 0264-410X. Publisher: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Applications of oxime chemistry are described for the efficient bioconjugation of proteins and polysaccharides for the preparation of conjugate vaccines. A number of approaches are described in this manuscript to functionalize, proteins and polysaccharides with aminooxy (AO) groups and aldehydes which could then be covalently linked to each other via oxime formation, without the need for reduction. By using limiting numbers of active groups on each component, the extent of inter- and intramolecular crosslinking Could be controlled. The approaches described are compatible and complementary to a number of chemistries currently used in conjugate vaccine synthesis. Oxime chemistry can be used to both simplify the synthesis of and increase yields of conjugate vaccines. Mice immunized with pneumococcal type 14 conjugates that were made using oxime chemistry mounted significant anti-polysaccharide immune responses. The primary immune response could be boosted, indicating that the polysaccharide conjugate had characteristics of a T cell dependent antigen. (c) 2005 Elsevier Ltd. All rights reserved.

L12 ANSWER 5 OF 24 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN DUPLICATE 1

2006309126 EMBASE Recombinant kallikrein expression: Site-specific integration for hK6 production in human cells. Heuze-Vourc'h N.; Ainciburu M.; Planque C.; Brillard-Bourdet M.; Ott C.; Jolivet-Reynaud C.; Courty Y.. N. Heuze-Vourc'h, INSERM, U618 'Proteases et Vectorisation Pulmonaires', F-37032 Tours, France. heuze_vourch@yahoo.fr. Biological

Chemistry Vol. 387, No. 6, pp. 687-695 1 Jun 2006.
Refs: 51.
ISSN: 1431-6730. E-ISSN: 1437-4315. CODEN: BICHF3
B3876687. Pub. Country: Germany. Language: English. Summary Language: English.
Entered STN: 20060801. Last Updated on STN: 20060801

AB Kallikreins have been implicated in carcinogenesis and are promising biomarkers for the diagnosis and follow-up of various cancers. To evaluate the functions and clinical interest of kallikreins, it is important to be able to produce them as recombinant proteins. Here we summarize the various strategies used to produce kallikreins, emphasizing their advantages and limitations. We also describe an approach to achieve high-level production of kallikreins, such as hK6, with correct folding and activity, combining an expression system with targeted transgene integration and an efficient cultivation device to increase yield, the CELLine bioreactor. This novel method for recombinant kallikrein production will be useful to study their bio-pathological functions and to develop antibodies. Copyright .COPYRGT. by Walter de Gruyter.

L12 ANSWER 6 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN

2006:856835 Disaggregation and refolding of aggregated monoclonal antibodies: using high hydrostatic pressure as an effective purification method. Hesterberg, Lyndal K.; Allan, Christian B. (BaroFold, Inc, Boulder, CO, 80304, USA). Abstracts of Papers, 232nd ACS National Meeting, San Francisco, CA, United States, Sept. 10-14, 2006, BIOT-075. American Chemical Society: Washington, D. C. (English) 2006. CODEN: 69IHRD.

AB Protein aggregates reduce yields, increase costs and can require specific downstream process steps during manufacturing High yielding expression systems for humanized monoclonal antibodies may generate significant levels of soluble aggregates (dimers, trimers, tetramers of the antibody) during cell culture production because of the high concentration of the antibodies and extended temps. at 37°C. Protein A/G affinity chromatog. is routinely used to sep. the antibody from host cell proteins and other components in the cell culture, either as a direct capture step or a polishing step in the downstream purification However, soluble aggregates of antibodies are not separated from monomers using Protein A/G chromatog. High Hydrostatic Pressure PreEMT (TM) technol. has been demonstrated to be a novel, inexpensive and effective alternative to traditional methods of aggregate removal by eliminating antibody aggregates directly without the need of an addnl. purification step and, in the same high pressure treatment step, increase yields of correctly folded antibody.

L12 ANSWER 7 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN

2004:754417 Document No. 141:256532 Soluble derivatives of human neutral hyaluronidase and their secretory manufacture for use in therapeutic modulation of glycosaminoglycan metabolism. Bookbinder, Louis H.; Kundu, Anirban; Frost, Gregory I. (Deliatroph Pharmaceuticals, Inc., USA). PCT Int. Appl. WO 2004078140 A2 20040916, 210 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, ML, MR, NE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US6656 20040305. PRIORITY: US 2003-452360P 20030305.

AB A variant of human neutral active hyaluronidase with improved solubility is

constructed and a cDNA encoding it is cloned for manufacture of the enzyme for use in the the treatment of glycosaminoglycan-associated pathologies. This variant of the enzyme lacks its hydrophobic C-terminal domain including the GPI anchor to improve solubility and increase yields of secreted activity. Minimally active domains of the enzyme, including asparagine-linked glycosidation required for a functional enzyme are identified. Secretory manufacture of the enzyme and the use of leader peptides that increase the efficiency of secretion of the enzyme are also described. The signal and leader peptide of the enzyme is unusually long and may play a role in limiting secretion by promotinq aggregation. Replacing it with the signal peptide of the mouse Ig κ chain increased yields of secreted enzyme by .apprx.6-fold. Modified forms of the enzyme, e.g. sialylated and PEGylated, with increased stability and serum pharmacokinetics over naturally occurring slaughterhouse enzymes are described. Further described are suitable formulations of a substantially purified recombinant sHASEGP glycoprotein derived from a eukaryotic cell that generate the proper glycosylation required for its optimal activity.

L12 ANSWER 8 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN

2003:511966 Document No. 139:80275 Polyvalent cation-sensing receptors in Atlantic salmon and use thereof in modulating responses of transgenic fish to environmental salinity. Harris, H. William; Nearing, Jacqueline; Betka, Marlies (Marical, LLC, USA). U.S. Pat. Appl. Publ. US 2003124657 A1 20030703, 140 pp., Cont.-in-part of U. S. Ser. No. 121,441, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2002-125772 20020418. PRIORITY: US 2000-240392P 20001012; US 2000-240003P 20001012; WO 2001-US31704 20011011; US 2002-121441 20020411.

AB Three genes for Polyvalent Cation-Sensing Receptors (PVCR) in Atlantic Salmon are cloned and characterized for use in engineering the ability of the fish to respond to changes in environmental salinity during development. These PVCR have been named SalmoKCaR#1, SalmoKCaR#2 (only one claimed), and SalmoKCaR#3. The genes can be used to speed the adaptation of young fish to living in seawater during smoltification and accelerate their growth. The present invention includes homologs thereof, antibodies thereto, and methods for assessing SalmoKCaR nucleic acid mols. and polypeptides. The present invention further includes plasmids, vectors, host cells containing the nucleic acid sequences of SalmoKCaR #1,2 and/or 3. The genes were identified by degenerate PCR using primers derived from a shark calcium channel gene. Tissue distribution of the mRNAs varied as a function of growth in saltwater vs. freshwater. Use of new methods to control polyvalent cation levels in the aquaculture of salmon are shown to improve growth and development and to increase yields is demonstrated.

L12 ANSWER 9 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN

2003:334505 Document No. 138:351367 Polyvalent cation-sensing receptor proteins of Salmo salar and its use in modulating responses to environmental salinity. Harris, H. William; Nearing, Jacqueline; Betka, Marlies (Marical, LLC, USA). U.S. Pat. Appl. Publ. US 2003082574 A1 20030501, 140 pp., Cont.-in-part of U. S. Ser. No. 121,441, abandoned. (English). CODEN: USXXCO. APPLICATION: US 2002-125778 20020418. PRIORITY: US 2000-240392P 20001012; US 2000-240003P 20001012; WO 2001-US31704 20011011; US 2002-121441 20020411.

AB Three genes for Polyvalent Cation-Sensing Receptors (PVCR) in Atlantic Salmon are cloned and characterized for use in engineering the ability of the fish to respond to changes in environmental salinity during development. These PVCR have been named SalmoKCaR#1, SalmoKCaR#2, and SalmoKCaR#3. The genes can be used to speed the adaptation of young fish to living in seawater during smoltification and accelerate their growth. Similarly, a knowledge of the adaptation to seawater can be used to develop feeding and growth practices that improve adaptation, survival, growth and widen the window for release of smolts into ocean waters. The

present invention includes homologs thereof, antibodies thereto, and methods for assessing SalmoKCaR nucleic acid mols. and polypeptides. The present invention further includes plasmids, vectors, host cells containing the nucleic acid sequences of SalmoKCaR #1,2 and/or 3. The genes were identified by degenerate PCR using primers derived from a shark calcium channel gene. Tissue distribution of the mRNAs varied as a function of growth in saltwater vs. freshwater. Use of new methods to control polyvalent cation levels in the aquaculture of salmon are shown to improve growth and development and to increase yields is demonstrated.

L12 ANSWER 10 OF 24 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

2003204377 EMBASE Design and selection of ligands for affinity chromatography. Labrou N.E.. N.E. Labrou, Laboratory of Enzyme Technology, Dept. of Agricultural Biotechnology, Agricultural University of Athens, 75 Iera Odos Street, GR-11855 Athens, Greece. lambrou@aua.gr. Journal of Chromatography B: Analytical Technologies in the Biomedical and Life Sciences Vol. 790, No. 1-2, pp. 67-78 25 Jun 2003.
Refs: 93.
ISSN: 1570-0232. CODEN: JCBAAI
Pub. Country: Netherlands. Language: English. Summary Language: English.
Entered STN: 20030605. Last Updated on STN: 20030605

AB Affinity chromatography is potentially the most selective method for protein purification. The technique has the purification power to eliminate steps, increase yields and thereby improve process economics. However, it suffers from problems regarding ligand stability and cost. Some of the most recent advances in this area have explored the power of rational and combinatorial approaches for designing highly selective and stable synthetic affinity ligands. Rational molecular design techniques, which are based on the ability to combine knowledge of protein structures with defined chemical synthesis and advanced computational tools, have made rational ligand design feasible and faster. Combinatorial approaches based on peptide and nucleic acid libraries have permitted the rapid synthesis of new synthetic affinity ligands of potential use in affinity chromatography. The versatility of these approaches suggests that, in the near future, they will become the dominant methods for designing and selection of novel affinity ligands with scale-up potential. .COPYRGT. 2003 Elsevier Science B.V. All rights reserved.

L12 ANSWER 11 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN

2001:713570 Document No. 135:270245 The corn fae2 gene involved in meristem proliferation and inflorescence development and use of the gene and promoter in plant breeding. Jackson, David P.; Taguchi Shiobara, Fumio; Hake, Sarah; Yuan, Zhuang (Cold Spring Harbor Laboratory, USA). PCT Int. Appl. WO 2001070987 A2 20010927, 73 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US8709 20010319. PRIORITY: US 2000-PV190160 20000317.

AB The invention relates to the isolation and characterization of a novel maize gene (fae2 (fasciated ear 2)) responsible for meristem proliferation and inflorescence development. The novel gene, gene product, and regulatory regions may be used to manipulate meristem growth, inflorescence development and arrangement, and ultimately to improve yield of plants. The invention includes the novel gene and protein product as

well as the use of the same for temporal and spatial expression in transgenic plants to enhance kernel development, alter plant morphol. and increase yield in plants. The gene was first identified as having an effect on fasciation of ears and the morphol. of the tassel. The gene was cloned after tagging with Mu; two Mu-tagged alleles were identified. The gene has no introns and appears to encode a member of the leucine-rich repeat family of transmembrane receptors.

L12 ANSWER 12 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN
2001:671093 Document No. 135:209935 Cosecretion of chaperones and low-molecular-size medium additives increases the yield of recombinant disulfide-bridged proteins. Schaffner, Jorg; Winter, Jeannette; Rudolph, Rainer; Schwarz, Elisabeth (Institut fur Biotechnologie, Martin-Luther-Universitat Halle-Wittenberg, Halle, 06120, Germany). Applied and Environmental Microbiology, 67(9), 3994-4000 (English) 2001. CODEN: AEMIDF. ISSN: 0099-2240. Publisher: American Society for Microbiology.
AB Attempts were made to engineer the periplasm of Escherichia coli to an expression compartment of heterologous proteins in their native conformation. As a first approach the low-mol.-size additive L-arginine and the redox compound glutathione (GSH) were added to the culture medium. Addition of 0.4 M L-arginine and 5 mM reduced GSH increased the yield of a native tissue-type plasminogen activator variant (rPA), consisting of the kringle-2 and the protease domain, and a single-chain antibody fragment (scFv) up to 10- and 37-fold, resp. A variety of other medium additives also had pos. effects on the yield of rPA. In a second set of expts., the effects of cosecreted ATP-independent mol. chaperones on the yields of native therapeutic proteins were investigated. At optimized conditions, cosecretion of E. coli DnaJ or murine Hsp25 increased the yield of native rPA by a factor of 170 and 125, resp. Cosecretion of DnaJ also dramatically increased the amount of a second model protein, native proinsulin, in the periplasm. The results of this study are anticipated to initiate a series of new approaches to increase the yields of native, disulfide-bridged, recombinant proteins in the periplasm of E. coli.

L12 ANSWER 13 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN
1998:640360 Document No. 129:271519 Vectors and methods for site-specific integration of transforming DNA in mammalian cells. Reff, Mitchell E.; Barnett, Richard Spence; McLachlan, Karen Retta (IDEC Pharmaceuticals Corp., USA). PCT Int. Appl. WO 9841645 A1 19980924, 114 pp. DESIGNATED STATES: W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US3935 19980309. PRIORITY: US 1997-819866 19970314.
AB A two step method for site specific integration of a desired DNA at a target site in a mammalian cell via homologous recombination is described. The method involves first transforming cells with DNA carrying a selectable marker allowing transformants to be screened for efficient expression of the integrated gene. Transformants showing high level expression are then transformed with a second vector designed to integrate into the first vector. Succesful integration leads to the formation of an intact copy of a gene for a second selectable marker allowing transformants to be directly screened for. The method minimizes background and maximizes expression of the foreign gene. It is particularly suitable for the preparation of mammalian cell lines secreting mammalian proteins at high levels, in particular Igs. Vectors and vector combinations for use in the method are also described. These vectors use prior art regulatory and nucleic acid-processing sequences in expression

cassettes. Use of the method to create histidinol-resistant CHO cells carrying a neomycin phosphotranferase gene that were then transformed with a plasmid targetted at the phosphotransferase sequences and carrying an expression cassette for an antibody to CD20 is demonstrated. Yields of 3.5 pg antibody/cell/day were obtained with peak yields of 4.9 pg antibody/cell/day. If the integrating DNA also contains a dihydrofolate reductase gene, the region can be amplified with methotrexate to further increase yields. Yields of 15-18 pg antibody/cell/day were obtained in a first round of amplification and increased to 55-60 pg antibody/cell/day in subsequent amplifications.

L12 ANSWER 14 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN
1996:721737 Document No. 126:4832 An acetyl CoA carboxylase cDNA from maize and its use in the preparation of herbicide-resistant plants and altering patterns of fatty acid synthesis. Gengenbach, Burle G.; Somers, David A.; Wyse, Donald L.; Gronwald, John W.; Egli, Margaret A.; Lutz, Sheila M. (Regents of the University of Minnesota, USA). PCT Int. Appl. WO 9631609 A2 19961010, 130 pp. DESIGNATED STATES: W: BR, CA, MX, RU, US; RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1996-US4625 19960404. PRIORITY: US 1995-417089 19950405.
AB A complete cDNA of maize acetyl CoA carboxylase is reported and methods of using the cDNA to confer herbicide tolerance or altering the oil content of plants are described. Expression of the cDNA in a plant host in a sense or an antisense orientation is used to increase herbicide tolerance or resistance. Similarly, these expression cassettes can be used to alter the oil content of a plant. The expression cassette can also be introduced into other host cells to increase yield of a plant acetyl CoA carboxylase so that crystallized enzyme can be used to screen and identify other herbicides that bind to and inhibit the enzyme. The enzyme is shown to be the site of action of sethoxydim and haloxyfop and sethoxydim-tolerant cell line was shown to have an altered carboxylase. Antisera to affinity-purified enzyme were used to screen a cDNA expression library in λgt11. A full-length cDNA and partial cDNAs for a number of isoenzymes were obtained.

L12 ANSWER 15 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN
1993:402491 Document No. 119:2491 Activator gene for macrolide biosynthesis. Rao, Ramachandra Nagaraja; Turner, Jan Ross (Eli Lilly and Co., USA). Eur. Pat. Appl. EP 524832 A2 19930127, 22 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, PT, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1992-306792 19920724. PRIORITY: US 1991-736178 19910726.
AB A gene (srmR) encoding a protein that increases the efficiency of transcription of genes involved in macrolide biosynthesis in Streptomyces ambofaciens is identified. The gene is used to increase levels of transcription of genes of macrolide biosynthesis to increase yields of these compds. in fermn and identification of similar genes (no data). The gene was cloned from a cosmid carrying the genes for spiramycin biosynthesis of Streptomyces by complementation of the gene after insertional inactivation.

L12 ANSWER 16 OF 24 CAPLUS COPYRIGHT 2007 ACS on STN
1992:446549 Document No. 117:46549 Method for obtaining recombinant surface antigen of hepatitis b virus (HBsAg) of higher immunogenic capacity and use thereof in a vaccine preparation. Mucio Gonzalez, Verena Lucila; Penton Arias, Eduardo; Palou Garcia, Manuel; Fontirrochi Escobar, Gluvel; Nazabal Galvez, Marcelo; Gonzalez Griego, Marta de Jesus; Beldarrain Iznaga, Alejandro; Pardron Gonzalez, Guillermo Julio; Ramirez Alvage, Victoria; et al. (Centro de Ingenieria Genetica y Biotecnologia (CIGB), Cuba). Eur. Pat. Appl. EP 480525 A2 19920415, 24 pp. DESIGNATED STATES:

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1991-202615 19911007. PRIORITY: CU 1990-155 19901008.

AB A process for recovering expressed HBsAg from Pichia pastoris cells comprises: (a) lysing the cells in buffer comprising a chaotropic agent, sucrose, and EDTA; (b) precipitating contaminants at acid pH; (c) subjecting the antigen to acid adsorption and alkaline desorption on diatomaceous earth; (d) immunoaffinity chromatog. of the antigen using monoclonal antibody ; (e) subjecting eluted antigen to heat treatment at 30-40°; (f) washing the antigen in an anion-exchange column with detergent; and (g) HPLC of eluted antigen in the presence of detergent. The process increases yield of pure HBsAg in a particulate form having high immunogenicity. Cloning and purification of HBsAg, production of monoclonal antibody, and preparation of vaccine are presented.

L12 ANSWER 17 OF 24 MEDLINE on STN DUPLICATE 2

92026871. PubMed ID: 1928712. [Recombinant erythropoietin in autologous blood donation]. Rekombiniertes Erythropoetin wahrend autologer Blutspenden. von Bormann B; Weidler B; Friedrich M; von Andrian-Werburg H. (Abteilungen fur Anaesthesiologie und Operative Intensivmedizin, St. Johannes-Hospital, Duisburg-Hamborn.) Der Anaesthesist, (1991 Jul) Vol. 40, No. 7, pp. 386-90. Journal code: 0370525. ISSN: 0003-2417. Pub. country: GERMANY: Germany, Federal Republic of. Language: German.

AB As a result of the AIDS crisis, public and physician pressure have increased the utilization of autologous blood products. Attitudes about homologous blood transfusion, however, have changed dramatically in recent years. A large segment of the population undergoing elective surgery is elderly and therefore has a significant incidence of cardiovascular disease and a slow response of the erythropoietic system when acute anemia occurs. However, preoperative autologous blood donation programs require 2-5 weeks to complete; the average yield is only 2.2 units per patient. As a consequence, autologous predonation is underused and homologous transfusion cannot be completely avoided in all patients. For several years recombinant human erythropoietin (rHuEPO) has been available and has been successfully used in the treatment of patients with renal anemia. This study evaluated the effect of r-HuEPO on patients with preoperative autologous blood collection. METHODS. Ten patients of both sexes scheduled for hip arthroplasty underwent a preoperative autologous program. During a period of 23 days prior to surgery autologous blood donation was performed with 7.5 ml/kg withdrawal on four occasions, the last one 5 days prior to surgery. Five patients were randomly treated with subcutaneous injections of rHuEPO (Erypo, Cilag GmbH, Sulzbach; Distributor: Fresenius AG, Oberursel, FRG) 200 IU/kg seven times, starting 3 days after the first blood withdrawal. All patients (n = 10) received oral iron therapy with iron sulphate 304 mg/die (= 100 mg iron/die). Patients with hypertension or recent myocardial infarction were excluded from the study. The hemoglobin level before donation had to be at least 11.0 g/dl. On each study day, a complete blood count and platelets, differential, and reticulocyte count were determined by standard methods as were transferrin, ferritin, and total iron-binding capacity. Blood loss and blood consumption during and after the operation were registered. The indication for blood transfusion (autologous/homologous) was based on hemoglobin values, which were not acceptable below 8.5 g/dl. RESULTS. No side effects of rHuEPO treatment were observed. Blood loss ranged from 650 to 1100 ml intraoperatively and 400 to 950 ml postoperatively with no differences between the groups. Patients with rHuEPO had no autologous red cell concentrates (aRCC) during the operation; two of them had two units of aRCC on the 2nd postoperative day. Two of the patients in the control group had intraoperative blood transfusions (2 and 3 units aRCC, respectively); all patients in this group were transfused postoperatively: 12 of the 20 units collected were utilized. At the onset of the operation

the mean hemoglobin value in patients with rHuEPO was 13.5 +/- 0.4 g/dl compared to 11.3 +/- 0.3 g/dl in the controls. Reticulocytes increased significantly during the investigation period. On the 2nd, 3rd, and 4th days of autologous blood collection and before the onset of surgery, the number of reticulocytes was significantly greater in rHuEPO patients than in the controls. Further laboratory variables such as transferrin, ferritin, and total iron-binding capacity did not change significantly during the investigation period; there were no significant differences between the two groups. DISCUSSION. The results of the present study show that rHuEPO leads to an increase in reticulocytes with maintenance of hemoglobin levels during the phlebotomy program. As a consequence, patients with anemia and particular contraindications to homologous blood derivatives (irregular antibodies, Jehovah's Witnesses) may be able to undergo major surgery successfully. The possibility of shortening the intervals between phlebotomies would seem to be of major advantage; our data also suggest that an aggressive autologous blood collection program would increase yields over present programs.
In our institute a minimum hemoglobin level of 11.5 g/dl is accepted for autologous donation.(ABSTRACT TRUNCATED AT 400 WORDS)

L12 ANSWER 18 OF 24 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
1990:10809 Document No.: PREV199038000109; BR38:109. USING ANTIBODIES TO INCREASE YIELDS. DIXON B [Reprint author]. LONDON, UK. Bio-Technology (New York), (1989) Vol. 7, No. 11, pp. 1118. CODEN: BTCHDA. ISSN: 0733-222X. Language: ENGLISH.

L12 ANSWER 19 OF 24 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
1989:568166 The Genuine Article (R) Number: AX105. LIVESTOCK PRODUCTION - USING ANTIBODIES TO INCREASE YIELDS. DIXON B. BIO-TECHNOLOGY (NOV 1989) Vol. 7, No. 11, pp. 1118-1118. ISSN: 0733-222X. Publisher: NATURE PUBLISHING CO, 345 PARK AVE SOUTH, NEW YORK, NY 10010-1707. Language: English.

L12 ANSWER 20 OF 24 MEDLINE on STN DUPLICATE 3
89231585. PubMed ID: 2714231. A method for recovery of native, clonally-restricted immunoglobulins from agarose gels. Janson R W; Vertosick F T Jr; Kelly R H. (Departments of Medicine, University of Pittsburgh School of Medicine, PA.) Electrophoresis, (1989 Jan) Vol. 10, No. 1, pp. 11-5. Journal code: 8204476. ISSN: 0173-0835. Pub. country: GERMANY, EAST: German Democratic Republic. Language: English.
AB Multiple low level, clonally-restricted, immunoglobulins (Ig) are commonly encountered on routine serum protein electrophoresis by clinical laboratories using high resolution zone electrophoresis on agarose. We sought a method for recovering the clonally-restricted Ig, in native configuration, from clinical laboratory gels as a first step in the investigation of its clinical significance. We found that a two-stage electrophoretic procedure gave consistently good recoveries. After routine agarose gel electrophoresis, portions of the electropherogram, containing clonally-restricted Ig, were excised and subjected to flatbed isoelectric focusing in agarose to enhance separation of the individual antibody clonotypes. Multiple slabs, containing the same clonally-restricted Ig, could be cut from adjacent tracks (i.e., tracks loaded with the same specimen) on the zone electropherogram and applied to a single track on the focusing gel to improve separation and increase yields. The focused gels were cut to isolate slabs containing individual clonotypes. These slabs were washed to remove carrier ampholytes and held at -20 degrees C overnight. Ig was extracted from the thawed gels, with 61-68% recovery, by ultracentrifugation following physical disruption of the gel. Antigen binding activity of the recovered Ig was verified by rate nephelometry. Clonally-restricted

antibodies were successfully isolated from an immune animal serum by this procedure and biotinylated for use as probes on Western biots.

L12 ANSWER 21 OF 24 MEDLINE on STN DUPLICATE 4
84263122. PubMed ID: 6235176. Comparison of various preparations of nuclear antigens by hemagglutination inhibition (HAI). Boak A M; Kincaid L A; Treadwell E L; McDonald P; Ellis K R; Sharp G C; Agris P F. Immunological communications, (1984) Vol. 13, No. 2, pp. 127-36. Journal code: 0353016. ISSN: 0090-0877. Pub. country: United States. Language: English.

AB A clinical laboratory carrying out tests for antinuclear antibodies requires an efficient, reliable preparation method to produce a high yield of nuclear antigens at low cost and a very sensitive, specific assay method for antigen activity. Various tissues were employed for preparation of small nuclear ribonucleoprotein (snRNP) and Sm antigens for these purposes. Fresh calf thymus cells and nuclei, commercially available calf and rabbit thymus acetone powders, fresh rat kidney and liver cells were used as sources of antigens prepared similarly by methods published previously. Preparations of antigens from whole calf thymus cell extracts were prepared with and without inhibitors to protease and RNase. snRNP and Sm antigens were assayed at each preparation step by hemagglutination inhibition (HAI). Using HAI it was possible to routinely assay snRNP and Sm at nanogram/ml quantities which was 10(6) fold more sensitive than Ouchterlony immunodiffusion. Results were expressed as relative specific activity as compared with calf thymus nuclear extract prepared by conventional methods. Protease and RNase inhibitors did not significantly increase yields. Thymus was the best source of snRNP and Sm. Fresh calf thymus extract produced a good, stable, reliable quantity of antigens, whereas calf and rabbit thymus acetone powders provided antigen at higher specific activity with less labor but slightly lower yields. Thus, considering the total cost of preparations, commercial sources may be superior to fresh sources in the clinical laboratory setting. These studies also revealed the utility of the sensitive HAI test not only in the clinical laboratory but also for further research endeavors.

L12 ANSWER 22 OF 24 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN
1982:130314 The Genuine Article (R) Number: NG282. ANTIBODY IN CULTURES OF PLASMODIUM-FALCIPARUM INCREASES YIELD OF MEROZOITE ANTIGENS. LYON J A (Reprint); HAYNES J D; PAVIA C A; DIGGS C L. WALTER REED ARMY INST RES, WASHINGTON, DC 20012. FEDERATION PROCEEDINGS (1982) Vol. 41, No. 3, pp. 585-585. ISSN: 0014-9446. Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998 USA. Language: English.

L12 ANSWER 23 OF 24 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
1982:119660 Document No.: PREV198223049652; BR23:49652. ANTIBODY IN CULTURES OF PLASMODIUM-FALCIPARUM INCREASES YIELD OF MEROZOITE ANTIGENS. LYON J A [Reprint author]; HAYNES J D; PAVIA C A; DIGGS C L. WALTER REED ARMY INST RES, WASHINGTON, DC 20012, USA. Federation Proceedings, (1982) Vol. 41, No. 3, pp. ABSTRACT 1841. Meeting Info.: 66TH ANNUAL MEETING OF THE FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY, NEW ORLEANS, LA., USA, APRIL 15-23, 1982. FED PROC.
CODEN: FEPRA7. ISSN: 0014-9446. Language: ENGLISH.

L12 ANSWER 24 OF 24 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN
81214887 EMBASE Document No.: 1981214887. Growth of 17D yellow fever virus in a macrophage-like cell line, U937: Role of Fc and viral receptors in

antibody-mediated infection. Schlesinger J.J.; Brandriss M.W.. Dept. Med., Univ. Rochester Sch. Med. Dent., N.Y., United States. Journal of Immunology Vol. 127, No. 2, pp. 659-665 1981. CODEN: JOIMA3 Pub. Country: United States. Language: English. Entered STN: 911209. Last Updated on STN: 911209

AB Growth characteristics of 17D yellow fever virus (17D-YF) and conditions for infection were studied in U937, a macrophage-like, Fc receptor-bearing continuous human cell line. Antibody to 17D-YF was obtained by immunization of normal subjects with 17D-YF vaccine. Cells were infected in the presence or absence of immune whole sera or immunoglobulin fractions. Infection of U937 was temperature dependent; the yield of virus was variable but at low temperature viral titers were consistently higher when infection was established in the presence of antibody . Results of infectious center assays indicated that the increased yield of virus was largely or entirely due to an increase yield in the number of cells producing virus early in the course of infection. Enhancement of viral growth was mediated by IgG but not IgM fractions of immune sera. Trypsinization of U937 resulted in a 90 to 95% reduction of infection in the absence of antibody but in the presence of antibody viral titers were higher in trypsinized than in nontrypsinized cells. Antibody to 17D-YF, contained in the whole IgG fraction of sera, bound to U937 to mediate infection without first being complexed to virus. Preincubation of U937 with IgG1 but not IgG2 myeloma proteins abrogated antibody-mediated infection. This result is compatible with the known affinities of U937 Fc receptors for specific subclasses of IgG and provides evidence for the role of the Fc receptors in antibody-mediated enhancement of viral growth. Persistent infection characterized by a lack of detectable cytopathogenic effect was established in long-term cultures of U937. This pattern of infection might be related to the unique effectiveness of the 17D-YF vaccine.

```
=> s heavy chain framework
L13         99 HEAVY CHAIN FRAMEWORK

=> s l13 and increase yield
L14          0 L13 AND INCREASE YIELD

=> s l13 and improved yield
L15          0 L13 AND IMPROVED YIELD

=> s l13 and improved folding efficiency
L16          0 L13 AND IMPROVED FOLDING EFFICIENCY

=> s substitution heavy chain FR1
L17          0 SUBSTITUTION HEAVY CHAIN FR1

=> s l13 and FR1
L18         12 L13 AND FR1

=> s l18 and yield
L19          0 L18 AND YIELD

=> s l13 and subgroup consensus sequence
L20          0 L13 AND SUBGROUP CONSENSUS SEQUENCE

=> s l13 and humanized
L21         30 L13 AND HUMANIZED

=> s l21 and HVR1
```

```
L22           0 L21 AND HVR1

=> s l21 and increased assembled
L23           0 L21 AND INCREASED ASSEMBLED

=> s method

=> s method making
L24       1417 METHOD MAKING

=> s l24 and antibod?
L25         34 L24 AND ANTIBOD?

=> s l25 and increased assembled antibody
L26           0 L25 AND INCREASED ASSEMBLED ANTIBODY

=> s increased assembled antibody
L27           0 INCREASED ASSEMBLED ANTIBODY

=> s improved folding effiency
L28           0 IMPROVED FOLDING EFFIENCY

=> s anti-VEGF
L29        3620 ANTI-VEGF

=> s l29 and humanized
L30         214 L29 AND HUMANIZED

=> s l30 and HVR1 consensus sequence
L31           0 L30 AND HVR1 CONSENSUS SEQUENCE

=> s l30 and increased yield
L32           0 L30 AND INCREASED YIELD

=> s anti-IgE
L33       10326 ANTI-IGE

=> s l33 and humanized
L34         523 L33 AND HUMANIZED

=> s l34 and increased yield
L35           0 L34 AND INCREASED YIELD

=> s l34 and improved folding
L36           0 L34 AND IMPROVED FOLDING

=> s l34 and yield
L37           3 L34 AND YIELD

=> dup remove l37
PROCESSING COMPLETED FOR L37
L38           2 DUP REMOVE L37 (1 DUPLICATE REMOVED)

=> d l38 1-2 cbib abs

L38  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2007 ACS on STN
2004:633952   Document No. 141:156117  Methods for producing and improving
     yield of humanized or chimeric antibodies and fragments
     in cell culture.  Simmons, Laura (Genentech, Inc., USA).  PCT Int. Appl.
     WO 2004065417 A2 20040805, 161 pp.  DESIGNATED STATES: W:  AE, AE, AG, AL,
     AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY,
     BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK,
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DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US1844 20040123. PRIORITY: US 2003-442484P 20030123.

AB The present invention provides methods for producing humanized antibodies and increasing the yield of antibodies and/or antigen binding fragments when produced in cell culture. The antibodies are anti-VEGF and anti-IgE antibodies. In one aspect of the invention, at least one framework region amino acid residue of the variable domain is substituted by a corresponding amino acid from a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain. In another aspect, an amino acid is placed at a position proximal to a cys residue that participates in an intrachain variable domain disulfide bond that corresponds to an amino acid found at that position in a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain.

L38 ANSWER 2 OF 2 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 1

1998:472908 Document No.: PREV199800472908. Spray-drying performance of a bench-top spray dryer for protein aerosol powder preparation. Maa, Yuh-Fun [Reprint author]; Nguyen, Phuong-Anh; Sit, Kin; Hsu, Chung C.. Pharm. Res. Dev., Genntech Inc., 1 DNA Way, South San Francisco, CA 94080, USA. Biotechnology and Bioengineering, (Nov. 5, 1998) Vol. 60, No. 3, pp. 301-309. print.
CODEN: BIBIAU. ISSN: 0006-3592. Language: English.

AB The objective of this work was to improve a bench-top spray dryer's efficiency in both production recovery and throughput for preparing protein aerosol powders. A Buchi mini-spray dryer was used to prepare the powders of recombinant humanized anti-IgE antibody. The resulting powder's physical properties such as particle size, residual moisture, and morphology, along with its recovery and production rate was the basis of this development work. Mass balance suggests that approximately 10-20% of powder was lost in the exhaust air, consisting primarily of particles less than 2 mum. Also, significant loss (20-30%) occurred in the cyclone. Attempts were made to improve product recovery in the receiving vessel using dual-cyclone configurations, different cyclone designs, cyclones with anti-static treatment, and different receiver designs. System modifications such as replacing the original bag-filter unit with a vacuum system effectively reduced drying air flow resistance, allowing the protein to be dried at a lower inlet air temperature and the production scale to be increased. We concluded that the modified spray-drying system is advantageous over the original bench-top spray dryer. This improvement will be beneficial to early-stage research and development involving high-valued protein powders.

=> d his

(FILE 'HOME' ENTERED AT 09:06:29 ON 31 AUG 2007)

FILE 'MEDLINE, EMBASE, BIOSIS, SCISEARCH, CAPLUS' ENTERED AT 09:06:52 ON 31 AUG 2007

L1 3015896 S ANTIBOD?
L2 5343 S L1 AND CONSENSUS SEQUENCE
L3 0 S L2 AND IMPROVED FOLDING EFFICIENCY
L4 0 S L2 AND INCREASE YIELD
L5 26327 S L1 AND SUBSTITUTION
L6 7 S L5 AND HEAVY CHAIN FRAMEWORK

```
L7             3 DUP REMOVE L6 (4 DUPLICATES REMOVED)
L8             2 S FRAMEWORK CONSENSUS SEQUENCE
L9             2 DUP REMOVE L8 (0 DUPLICATES REMOVED)
L10         4363 S INCREASE YIELD
L11           32 S L10 AND ANTIBOD?
L12           24 DUP REMOVE L11 (8 DUPLICATES REMOVED)
L13           99 S HEAVY CHAIN FRAMEWORK
L14            0 S L13 AND INCREASE YIELD
L15            0 S L13 AND IMPROVED YIELD
L16            0 S L13 AND IMPROVED FOLDING EFFICIENCY
L17            0 S SUBSTITUTION HEAVY CHAIN FR1
L18           12 S L13 AND FR1
L19            0 S L18 AND YIELD
L20            0 S L13 AND SUBGROUP CONSENSUS SEQUENCE
L21           30 S L13 AND HUMANIZED
L22            0 S L21 AND HVR1
L23            0 S L21 AND INCREASED ASSEMBLED
L24         1417 S METHOD MAKING
L25           34 S L24 AND ANTIBOD?
L26            0 S L25 AND INCREASED ASSEMBLED ANTIBODY
L27            0 S INCREASED ASSEMBLED ANTIBODY
L28            0 S IMPROVED FOLDING EFFIENCY
L29         3620 S ANTI-VEGF
L30          214 S L29 AND HUMANIZED
L31            0 S L30 AND HVR1 CONSENSUS SEQUENCE
L32            0 S L30 AND INCREASED YIELD
L33        10326 S ANTI-IGE
L34          523 S L33 AND HUMANIZED
L35            0 S L34 AND INCREASED YIELD
L36            0 S L34 AND IMPROVED FOLDING
L37            3 S L34 AND YIELD
L38            2 DUP REMOVE L37 (1 DUPLICATE REMOVED)

=> s l1 and improv?
L39       115162 L1 AND IMPROV?

=> s l39 and yield
L40         3203 L39 AND YIELD

=> s l40 and framework
L41           81 L40 AND FRAMEWORK

=> s l41 and consensus sequence
L42            7 L41 AND CONSENSUS SEQUENCE

=> dup remove l42
PROCESSING COMPLETED FOR L42
L43            3 DUP REMOVE L42 (4 DUPLICATES REMOVED)

=> d 143 1-3 cbib abs

L43  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2007 ACS on STN
2004:633952   Document No. 141:156117  Methods for producing and
     improving yield of humanized or chimeric
     antibodies and fragments in cell culture.  Simmons, Laura
     (Genentech, Inc., USA).  PCT Int. Appl. WO 2004065417 A2 20040805, 161 pp.
     DESIGNATED STATES: W:  AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ,
     BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR,
     CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES,
     FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP,
     KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT,
     LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI.  (English).
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CODEN: PIXXD2. APPLICATION: WO 2004-US1844 20040123. PRIORITY: US 2003-442484P 20030123.

AB The present invention provides methods for producing humanized antibodies and increasing the yield of antibodies and/or antigen binding fragments when produced in cell culture. The antibodies are anti-VEGF and anti-IgE antibodies. In one aspect of the invention, at least one framework region amino acid residue of the variable domain is substituted by a corresponding amino acid from a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain. In another aspect, an amino acid is placed at a position proximal to a cys residue that participates in an intrachain variable domain disulfide bond that corresponds to an amino acid found at that position in a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain.

L43 ANSWER 2 OF 3 MEDLINE on STN

2003068504. PubMed ID: 12578364. Structure-based improvement of the biophysical properties of immunoglobulin VH domains with a generalizable approach. Ewert Stefan; Honegger Annemarie; Pluckthun Andreas. (Biochemisches Institut, Universitat Zurich, Winterthurerstrasse 190, CH-8057 Zurich, Switzerland.) Biochemistry, (2003 Feb 18) Vol. 42, No. 6, pp. 1517-28. Journal code: 0370623. ISSN: 0006-2960. Pub. country: United States. Language: English.

AB In a systematic study of V gene families carried out with consensus V(H) and V(L) domains alone and in combinations in the scFv format, we found comparatively low expression yields and lower cooperativity in equilibrium unfolding in antibody fragments containing V(H) domains of human germline families 2, 4, and 6. From an analysis of the packing of the hydrophobic core, the completeness of charge clusters, the occurrence of unsatisfied hydrogen bonds, and residues with low beta-sheet propensities, positive Phi angles, and exposed hydrophobic side chains, we pinpointed residues potentially responsible for the unsatisfactory properties of these germline-encoded sequences. Several of those are in common between the domains of the even-numbered subgroups, but do not occur in the odd-numbered ones. In this study, we have systematically exchanged those residues alone and in combination in two different scFvs using the V(H)6 framework, and we describe their effect on equilibrium stability and folding yield. We improved the stability by 20.9 kJ/mol and the expression yield by a factor of 4 and can now use these data to rationally engineer antibodies derived from this and similar germline families for better biophysical properties. Furthermore, we provide an improved design for libraries exploiting the significant additional diversity provided by these frameworks. Both antibodies studied here completely retain their binding affinity, demonstrating that the CDR conformations were not affected.

L43 ANSWER 3 OF 3 MEDLINE on STN DUPLICATE 1

2002737160. PubMed ID: 12498801. Biophysical properties of human antibody variable domains. Ewert Stefan; Huber Thomas; Honegger Annemarie; Pluckthun Andreas. (Biochemisches Institut, Universitat Zurich, Winterthurerstr 190, CH-8057 Zurich, Switzerland.) Journal of molecular biology, (2003 Jan 17) Vol. 325, No. 3, pp. 531-53. Journal code: 2985088R. ISSN: 0022-2836. Pub. country: England: United Kingdom. Language: English.

AB There are great demands on the stability, expression yield and resistance to aggregation of antibody fragments. To untangle intrinsic domain effects from domain interactions, we present first a systematic evaluation of the isolated human immunoglobulin variable heavy

(V(H)) and light (V(L)) germline family consensus domains and then a systematic series of V(H)-V(L) combinations in the scFv format. The constructs were evaluated in terms of their expression behavior, oligomeric state in solution and denaturant-induced unfolding equilibria under non-reducing conditions. The seven V(H) and seven V(L) domains represent the consensus sequences of the major human germline subclasses, derived from the Human Combinatorial Antibody Library (HuCAL). The isolated V(H) and V(L) domains with the highest thermodynamic stability and yield of soluble protein were V(H)3 and V(kappa)3, respectively. Similar measurements on all domain combinations in scFv fragments allowed the scFv fragments to be classified according to thermodynamic stability and in vivo folding yield. The scFv fragments containing the variable domain combinations H3kappa3, H1b kappa3, H5kappa3 and H3kappa1 show superior properties concerning yield and stability. Domain interactions diminish the intrinsic differences of the domains. ScFv fragments containing V(lambda) domains show high levels of stability, even though V(lambda) domains are surprisingly unstable by themselves. This is due to a strong interaction with the V(H) domain and depends on the amino acid sequence of the CDR-L3. On the basis of these analyses and model structures, we suggest possibilities for further improvement of the biophysical properties of individual frameworks and give recommendations for library design.
Copyright 2003 Elsevier Science Ltd.

```
=> s (simmons l?/au)
L44       1221 (SIMMONS L?/AU)

=> s l44 and yield
L45          7 L44 AND YIELD

=> dup remove l45
PROCESSING COMPLETED FOR L45
L46           5 DUP REMOVE L45 (2 DUPLICATES REMOVED)

=> d 146 1-5 cbib abs

L46  ANSWER 1 OF 5  BIOSIS  COPYRIGHT (c) 2007 The Thomson Corporation  on STN
     DUPLICATE 1
2006:510675  Document No.: PREV200600496123. A model of pecan tree growth for
     the management of pruning and irrigation. Andales, Allan; Wang, Junming
     [Reprint Author]; Sammis, Ted W.; Mexal, John G.; Simmons, Luke J.
     ; Miller, David R.; Gutschick, Vince P.. New Mexico State Univ, Dept Plant
     and Environm Sci, MSC3Q BOX30003, Las Cruces, NM 88003 USA.
     jwang@weather.nmsu.edu. Agricultural Water Management, (JUL 16 2006) Vol.
     84, No. 1-2, pp. 77-88.
     ISSN: 0378-3774. Language: English.
AB   Pecans [Carya illinoensis (Wangenh.) C.  Koch] are an important cash crop
     in and southwestern USA.  The pecan is an alternate bearing tree and its
     water use is greater than that of most row crops.  Irrigation, pruning
     amount, and timing must be effectively managed to reduce alternate bearing
     for maximum profits.  A simulation model of pecan growth and yield
     is a potential tool for managing irrigation and pruning amounts and
     timing.  An object-based pecan growth model was developed and validated to
     simulate daily pecan tree dry matter production, biomass allocation to
     leaves, nuts, trunk, and branches, and alternate bearing according to
     inputs of weather data, soil condition, irrigation, and pruning
     operations.  Daily dry matter production per unit of evapotranspiration
     (water use efficiency) was calculated as a function of average vapor
     pressure deficit.  Biomass allocation functions were derived from tree
     growth measurements at an orchard near Las Cruces, NM.  Alternate bearing
```

was simulated as a function of the level of root starch reserves. it was theorized that the setting of pistillate flowers and subsequent nut yields are proportional to the level of root starch reserves in the preceding dormant phase (winter). Mathematical functions for the effects of irrigation and pruning on tree growth and yield were derived from the literature and available data. The model was calibrated using 2002, historical, and literature data and validated against 2003 and 2004 data obtained from a mature pecan (Western Schley cultivar) orchard near Las Cruces, NM. Overall accuracy was above 89% for simulated total dry matter production, nut yield, tree height, and diameter at breast height (DBH). This model was found to adequately simulate the effects of climate, irrigation, and pruning on pecan tree growth, nut yield, and alternate bearing. It can potentially be used to schedule and estimate the amount of irrigation and pruning to optimize pecan nut yield. (c) 2006 Elsevier B.V. All rights reserved.

L46 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
2004:633952 Document No. 141:156117 Methods for producing and improving yield of humanized or chimeric antibodies and fragments in cell culture. Simmons, Laura (Genentech, Inc., USA). PCT Int. Appl. WO 2004065417 A2 20040805, 161 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US1844 20040123. PRIORITY: US 2003-442484P 20030123.
AB The present invention provides methods for producing humanized antibodies and increasing the yield of antibodies and/or antigen binding fragments when produced in cell culture. The antibodies are anti-VEGF and anti-IgE antibodies. In one aspect of the invention, at least one framework region amino acid residue of the variable domain is substituted by a corresponding amino acid from a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain. In another aspect, an amino acid is placed at a position proximal to a cys residue that participates in an intrachain variable domain disulfide bond that corresponds to an amino acid found at that position in a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain.

L46 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2007 ACS on STN
2001:12626 Document No. 134:91089 Improved fermentative yield, chromatographic recovery, and stability of Apo-2 ligand using divalent metal ions. Ashkenazi, Avi J.; Hymowitz, Sarah; Kelley, Robert F.; Koumenis, Iphegeni; Leung, Susan; O'connell, Mark; Pai, Roger; Shahrokh, Zahra; Simmons, Laura (Genentech, Inc., USA). PCT Int. Appl. WO 2001000832 A1 20010104, 60 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US17579 20000626. PRIORITY: US 1999-PV141342 19990628.
AB Methods of making Apo-2 ligand (Apo-2L, also known as TRAIL or tumor-necrosis factor-related apoptosis-inducing ligand) and formulations of Apo-2L using divalent metal ions are provided. Such divalent metal ions include zinc and cobalt which improve Apo-2L trimer formation and

stability. The crystal structure of Apo-2L is also provided, along with Apo-2 ligand variant polypeptides with improved stability, identified using oligonucleotide-directed mutagenesis. Replicable plasmid vectors are described for cloning and expression of Apo-2L and its variants in host Escherichia coli.

L46 ANSWER 4 OF 5 SCISEARCH COPYRIGHT (c) 2007 The Thomson Corporation on STN

1992:302457 The Genuine Article (R) Number: HT165. TOPOLOGICAL KINKS IN PHI(2N) FIELD-THEORIES - A VARIATIONAL APPROACH. COOPER F (Reprint); SIMMONS L M; SODANO P. UNIV CALIF LOS ALAMOS SCI LAB, DIV THEORET, LOS ALAMOS, NM 87545 (Reprint); UNIV CALIF LOS ALAMOS SCI LAB, CTR NONLINEAR STUDIES, LOS ALAMOS, NM 87545; UNIV PERUGIA, SEZ IST NAZL FIS NUCL, I-06100 PERUGIA, ITALY; UNIV PERUGIA, DIPARTIMENTO FIS, I-06100 PERUGIA, ITALY; SANTA FE INST, SANTA FE, NM 87501. PHYSICA D (APR 1992) Vol. 56, No. 1, pp. 68-83. ISSN: 0167-2789. Publisher: ELSEVIER SCIENCE BV , PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The delta-expansion and the linear delta-expansion are analytical perturbation techniques that enable one to find approximate analytic solutions to nonlinear problems. These expansions, augmented by new variational strategies, often yield excellent results already in first order. We study in this paper the static kinks in scalar field theories with V[phi] = - 1/2m2-phi-2 + g-phi-2n using these techniques. We find excellent agreement between the lowest order variational approximation in both methods and the exact answer. We also estimate the energy of the first excited quantum state by considering small oscillations about the kink motion and using our variational wave functions and a shape parameter ansatz for the first excited state wave function.

L46 ANSWER 5 OF 5 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN DUPLICATE 2

1980:141067 Document No.: PREV198069016063; BA69:16063. WIDTH WEIGHT ENDOSPERM AND BRAN OF THE WHEAT GRAIN AS DETERMINANTS OF FLOUR MILLING YIELD IN NORMAL AND SHRIVELLED WHEATS. SIMMONS L [Reprint author]; MEREDITH P. DEP SCI IND RES, WHEAT RES INST, CHRISTCHURCH, NZ. New Zealand Journal of Science, (1979) Vol. 22, No. 1, pp. 1-10. CODEN: NZJSAB. ISSN: 0028-8365. Language: ENGLISH.

AB In normal wheat grains of 5 cultivars and frost-shrivelled grains of 2 cultivars, length, width, thickness, wt, volume, proportion of endosperm and yield of flour in an experimental mill were measured. Kernel width may be used as a simple field technique to estimate kernel weight In normal grains, kernel wt gives a useful prediction of flour yield, but this is not applicable for frost-shrivelled grains or for those cultivars that yield "fluffy" flours. It is suggested that frosting prevents or slows the processes of pericarp degradation so that frosted grains have a greater relative amount of bran. Shrivelled grains may be distinguished from sound grains, regardless of size and texture, by low content of endosperm, low specific gravity and high ratio of length to width.

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CA SUBSCRIBER PRICE	-15.60	-15.60

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NEWS	3	OCT 19	BEILSTEIN updated with new compounds
NEWS	4	NOV 15	Derwent Indian patent publication number format enhanced
NEWS	5	NOV 19	WPIX enhanced with XML display format
NEWS	6	NOV 30	ICSD reloaded with enhancements
NEWS	7	DEC 04	LINPADOCDB now available on STN
NEWS	8	DEC 14	BEILSTEIN pricing structure to change
NEWS	9	DEC 17	USPATOLD added to additional database clusters
NEWS	10	DEC 17	IMSDRUGCONF removed from database clusters and STN
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NEWS	12	DEC 17	TOXCENTER enhanced with 2008 MeSH vocabulary in MEDLINE segment
NEWS	13	DEC 17	MEDLINE and LMEDLINE updated with 2008 MeSH vocabulary
NEWS	14	DEC 17	CA/CAplus enhanced with new custom IPC display formats
NEWS	15	DEC 17	STN Viewer enhanced with full-text patent content from USPATOLD
NEWS	16	JAN 02	STN pricing information for 2008 now available
NEWS	17	JAN 16	CAS patent coverage enhanced to include exemplified prophetic substances
NEWS	18	JAN 28	USPATFULL, USPAT2, and USPATOLD enhanced with new custom IPC display formats
NEWS	19	JAN 28	MARPAT searching enhanced
NEWS	20	JAN 28	USGENE now provides USPTO sequence data within 3 days of publication
NEWS	21	JAN 28	TOXCENTER enhanced with reloaded MEDLINE segment
NEWS	22	JAN 28	MEDLINE and LMEDLINE reloaded with enhancements
NEWS	23	FEB 08	STN Express, Version 8.3, now available
NEWS	24	FEB 20	PCI now available as a replacement to DPCI
NEWS	25	FEB 25	IFIREF reloaded with enhancements
NEWS	26	FEB 25	IMSPRODUCT reloaded with enhancements

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                  U.S. National Patent Classification

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FILE 'HOME' ENTERED AT 18:49:23 ON 12 MAR 2008

=>
=> file medline embase biosis scisearch caplus
COST IN U.S. DOLLARS                                 SINCE FILE      TOTAL
                                                        ENTRY    SESSION
FULL ESTIMATED COST                                      0.21       0.21

FILE 'MEDLINE' ENTERED AT 18:49:40 ON 12 MAR 2008

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=> s method improving
L1         400 METHOD IMPROVING

=> s l1 and humanized antibody
L2           0 L1 AND HUMANIZED ANTIBODY

=> s l1 and improved antibody yield
L3           0 L1 AND IMPROVED ANTIBODY YIELD

=> s l1 and antibod?
L4           4 L1 AND ANTIBOD?

=> s l4 and yield
L5           0 L4 AND YIELD

=> dup remove l4
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PROCESSING COMPLETED FOR L4
L6             4 DUP REMOVE L4 (0 DUPLICATES REMOVED)

=> s l6 and pd<20030123
   1 FILES SEARCHED...
   4 FILES SEARCHED...
L7             2 L6 AND PD<20030123

=> d l7 1-2 cbib abs

L7   ANSWER 1 OF 2  BIOSIS  COPYRIGHT (c) 2008 The Thomson Corporation  on STN
1989:220117  Document No.: PREV198987111734; BA87:111734. IMMUNOENZYMATIC
     LABELLING PATTERN OF DIHYDROFOLATE REDUCTASE USING ALKALINE
     PHOSPHATASE-ANTI-ALKALINE PHOSPHATASE APAAP METHOD IN HEMIC CELLS. NANO R
     [Reprint author]; REZZANI R; RODELLA L; GERZELLI G. DEP OF ANIMAL BIOL,
     CENT OF STUDY FOR HISTOCHEM, CNR, UNIV OF PAVIA, PIAZZA BOTTA 10, 27100
     PAVIA, ITALY. Acta Histochemica et Cytochemica, (1988) Vol. 21,
     No. 5, pp. 499-506.
     CODEN: ACHCBO. ISSN: 0044-5991. Language: ENGLISH.
AB   The availability fo anti-human dihydrofolate reductase polyclonal
     antibodies, allowed us to develop an immunohistochemical
     method improving the tetrazolium salt method for the
     demonstration of dihydrofolate reductase in samples in peripheral blood
     and bone marrow.  This enzyme, immunohistochemically demonstrated with the
     alkaline-phosphatase/anti-alkaline-phosphatase (APAAP) method,
     progressively increased during the normal differentiation of the
     granulocytopoietic series while it decreased in the erythropoietic series.
     The lymphocytes showed various positivity patterns which related to their
     subpopulations.  These results were in agreement with previous
     observations by the tetrazolium salt method.  Dihydrofolate reductase may
     be a useful marer in the study of granulocytic and lymphocytic cell
     lineages.

L7   ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
1998:543214  Document No. 129:158856  Improving performance of binding assays
     by use of more than one label.  Piran, Uri; Quinn, John J. (Chiron
     Diagnostics Corporation, USA).  PCT Int. Appl. WO 9834109 A1
     19980806, 30 pp.  DESIGNATED STATES: W:  AL, AM, AT, AU, AZ, BA,
     BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU,
     IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK,
     MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR,
     TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW:
     AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FI, FR, GA, GB, GR, IE,
     IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG.  (English).  CODEN:
     PIXXD2.  APPLICATION: WO 1998-IB125 19980202.  PRIORITY: US 1997-791591
     19970131.
AB   Novel binding assay techniques have been developed which improve accuracy
     and sensitivity via accounting for interfering factors.  They rely on use,
     in a simultaneous incubation, of two or more different labels, some of
     which are used primarily to detect analyte, and others to detect
     interfering substances originating in the sample.  The math. relationships
     between the labels allow corrections that lead to more accurate and
     sensitive determination of the presence and concentration of the analyte.  A
     triiodothyronine (T3) competitive immunoassay used di-Me acridinium
     ester-labeled monoclonal antibody to T3, long emission
     acridinium ester-labeled monoclonal antibody to T2, and bovine
     gamma globulin-T2 immobilized on paramagnetic particles.  Diluted goat
     anti-mouse IgG serum was used as a model for an interfering factor.


=> s antibod?
L8     3089192 ANTIBOD?
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```
=> s l8 and aligning hypervariable region
L9            0 L8 AND ALIGNING HYPERVARIABLE REGION

=> s l8 and aligning
L10         223 L8 AND ALIGNING

=> s l10 and hypervariable region
L11           5 L10 AND HYPERVARIABLE REGION

=> s l11 and framework substitution
L12           0 L11 AND FRAMEWORK SUBSTITUTION

=> s l11 and substitut?
L13           0 L11 AND SUBSTITUT?

=> s l11 and improve yield
L14           0 L11 AND IMPROVE YIELD

=> dup remove l11
PROCESSING COMPLETED FOR L11
L15            1 DUP REMOVE L11 (4 DUPLICATES REMOVED)

=> d l15 cbib abs

L15  ANSWER 1 OF 1     MEDLINE on STN                  DUPLICATE 1
1998308025.    PubMed ID: 9642095.   Automated classification of
     antibody complementarity determining region 3 of the heavy chain
     (H3) loops into canonical forms and its application to protein structure
     prediction. Oliva B; Bates P A; Querol E; Aviles F X; Sternberg M J.
     (Universitat Autonoma de Barcelona, 08193 Bellaterra, Barcelona, Spain. )
     Journal of molecular biology, (1998 Jun 26) Vol. 279, No. 5, pp. 1193-210.
     Journal code: 2985088R. ISSN: 0022-2836. Pub. country: ENGLAND: United
     Kingdom. Language: English.
AB   A computer-based algorithm was used to cluster the loops forming the
     complementarity determining region (CDR) 3 of the heavy chain (H3) into
     canonical classes.  Previous analyses of the three-dimensional structures
     of CDR loops (also known as the hypervariable regions)
     within antibody immunoglobulin variable domains have shown that
     for five of the six CDRs there are only a few main-chain conformations
     (known as canonical forms) that show clear relationships between sequence
     and structure.  However, the larger variation in length and conformation
     of loops within H3 has limited the classification of these loops into
     canonical forms.  The clustering procedure presented here is based on
     aligning the Ramachandran-coded main-chain conformation of the
     residues using a dynamic algorithm that allows the insertion of gaps to
     obtain an optimum alignment.  A total of 41 H3 loops out of 62
     non-identical loops, extracted from the Brookhaven Protein Data Bank, have
     been automatically grouped into 22 clusters.  Inspection of the clusters
     for consensus sequences or intra-loop interactions or invariant
     conformation led to the proposal of 13 canonical forms representing 31
     loops.  These canonical forms include a consideration of the geometry of
     both the take-off region adjacent to the bracing beta-strands and the
     remaining loop apex.  Subsequently a new set of 15 H3 loops not included
     in the initial analysis was considered.  The clustering procedure was
     repeated and nine of these 15 loops could be assigned to original
     clusters, including seven to canonical forms.  A sequence profile was
     generated for each canonical form from the original set of loops and
     matched against the sequences of the new H3 loops.  For five out of the
     seven new H3 loops that were in a canonical form, the correct form was
     identified at first rank by this predictive scheme.
     Copyright 1998 Academic Press.
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=> s l8 and production
L16     295340 L8 AND PRODUCTION

=> s l16 and increase yield
L17          8 L16 AND INCREASE YIELD

=> dup remove l17
PROCESSING COMPLETED FOR L17
L18          5 DUP REMOVE L17 (3 DUPLICATES REMOVED)

=> s l18 and pd<20030123
   2 FILES SEARCHED...
L19          2 L18 AND PD<20030123

=> d l19 1-2 cbib abs

L19  ANSWER 1 OF 2  SCISEARCH  COPYRIGHT (c) 2008 The Thomson Corporation  on
     STN
1989:568166   The Genuine Article (R) Number: AX105. LIVESTOCK
     PRODUCTION - USING ANTIBODIES TO INCREASE
     YIELDS.  DIXON B. BIO-TECHNOLOGY (NOV 1989) Vol. 7, No.
     11, pp. 1118-1118. ISSN: 0733-222X. Publisher: NATURE PUBLISHING CO, 345
     PARK AVE SOUTH, NEW YORK, NY 10010-1707. Language: English.

L19  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
1992:446549   Document No. 117:46549  Method for obtaining recombinant surface
     antigen of hepatitis b virus (HBsAg) of higher immunogenic capacity and
     use thereof in a vaccine preparation.  Mucio Gonzalez, Verena Lucila;
     Penton Arias, Eduardo; Palou Garcia, Manuel; Fontirrochi Escobar, Giuvel;
     Nazabal Galvez, Marcelo; Gonzalez Griego, Marta de Jesus; Beldarrain
     Iznaga, Alejandro; Pardron Gonzalez, Guillermo Julio; Ramirez Alvage,
     Victoria; et al. (Centro de Ingenieria Genetica y Biotecnologia (CIGB),
     Cuba).  Eur. Pat. Appl. EP 480525 A2 19920415, 24 pp.
     DESIGNATED STATES: R:  AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL,
     SE.  (English).  CODEN: EPXXDW.  APPLICATION: EP 1991-202615 19911007.
     PRIORITY: CU 1990-155 19901008.
AB   A process for recovering expressed HBsAg from Pichia pastoris cells
     comprises: (a) lysing the cells in buffer comprising a chaotropic agent,
     sucrose, and EDTA; (b) precipitating contaminants at acid pH; (c) subjecting
the
     antigen to acid adsorption and alkaline desorption on diatomaceous earth; (d)
     immunoaffinity chromatog. of the antigen using monoclonal antibody
     ; (e) subjecting eluted antigen to heat treatment at 30-40°; (f)
     washing the antigen in an anion-exchange column with detergent; and (g)
     HPLC of eluted antigen in the presence of detergent.  The process
     increases yield of pure HBsAg in a particulate form
     having high immunogenicity.  Cloning and purification of HBsAg, prodn
     . of monoclonal antibody, and preparation of vaccine are presented.


=> d l19 2 cbib abs

L19  ANSWER 2 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
1992:446549   Document No. 117:46549  Method for obtaining recombinant surface
     antigen of hepatitis b virus (HBsAg) of higher immunogenic capacity and
     use thereof in a vaccine preparation.  Mucio Gonzalez, Verena Lucila;
     Penton Arias, Eduardo; Palou Garcia, Manuel; Fontirrochi Escobar, Giuvel;
     Nazabal Galvez, Marcelo; Gonzalez Griego, Marta de Jesus; Beldarrain
     Iznaga, Alejandro; Pardron Gonzalez, Guillermo Julio; Ramirez Alvage,
     Victoria; et al. (Centro de Ingenieria Genetica y Biotecnologia (CIGB),
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Cuba). Eur. Pat. Appl. EP 480525 A2 19920415, 24 pp.
DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE. (English). CODEN: EPXXDW. APPLICATION: EP 1991-202615 19911007.
PRIORITY: CU 1990-155 19901008.

AB A process for recovering expressed HBsAg from Pichia pastoris cells comprises: (a) lysing the cells in buffer comprising a chaotropic agent, sucrose, and EDTA; (b) precipitating contaminants at acid pH; (c) subjecting the antigen to acid adsorption and alkaline desorption on diatomaceous earth; (d) immunoaffinity chromatog. of the antigen using monoclonal antibody ; (e) subjecting eluted antigen to heat treatment at 30-40°; (f) washing the antigen in an anion-exchange column with detergent; and (g) HPLC of eluted antigen in the presence of detergent. The process increases yield of pure HBsAg in a particulate form having high immunogenicity. Cloning and purification of HBsAg, prodn . of monoclonal antibody, and preparation of vaccine are presented.

=> s l16 and framework substitution
L20 1 L16 AND FRAMEWORK SUBSTITUTION

=> d l20 cbib abs

L20 ANSWER 1 OF 1 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN

1980150939 EMBASE Structural studies on induced antibodies with defined idiotypic specificities. IX. Framework differences in the heavy- and light-chain-variable regions of monoclonal anti-p-azophenylarsonate antibodies from A/J mice differing with respect to a cross-reactive idiotype. Estess P.; Lamoyi E.; Nisonoff A.; Capra J.D.. Dept. Microbiol., Univ. Texas Hlth Sci. Cent., Dallas. Tex. 75235, United States. Journal of Experimental Medicine Vol. 151, No. 4, pp. 863-875 1980.
ISSN: 0022-1007. CODEN: JEMEAV
Pub. Country: United States. Language: English.
Entered STN: 911209. Last Updated on STN: 911209

AB Amino terminal amino acid sequence analyses have been performed on the heavy and light chains of induced monoclonal antibodies with specificity for the hapten p-azophenylarsonate. Four of the eight antibodies react with conventional antisera to the previously described A/J anti-arsonate cross-reactive idiotype (CRI). Of the 16 chains analyzed, all but one contain sequence differences in their first framework segment (residues 1-30) that distinguish them from the heavy- and light-chain sequences found in anti-arsonate antibodies isolated from A/J serum or ascites fluid. The presence of such framework differences appears to be independent of whether or not the hybridoma antibodies bear the CRI. In spite of the framework substitutions, all four of the CRI-positive hybridoma antibodies have variable (V)-region frameworks that are very similar to each other and to the CRI-positive molecules found in A/J serum. Two of the four CRI-negative molecules are also structurally similar to the serum antibodies. Two others, however, are strikingly different from any serum anti-arsonate antibody thus far described and appear to reflect a completely separate repertoire of anti-arsonate antibodies in the A/J mouse. In addition, serological analyses with an anti-idiotypic antiserum generated against a CRI-positive hybridoma product suggested that each monoclonal antibody may possess individual antigenic specificities different from the determinant(s) detected with the conventional rabbit anti-CRI. The consistent appearance of framework substitutions in what has been thought to be a homogeneous antibody population has important implications for our understanding of the generation of

antibody diversity and for the precise chemical definition of an idiotype.

```
=> s l16 and improved yield
L21         44 L16 AND IMPROVED YIELD

=> s l21 and substitution
L22          0 L21 AND SUBSTITUTION

=> s l21 and modified framework
L23          0 L21 AND MODIFIED FRAMEWORK

=> s l21 and variable domain
L24          0 L21 AND VARIABLE DOMAIN

=> s l21 and consensus sequence
L25          0 L21 AND CONSENSUS SEQUENCE

=> s l21 and humanized antibod?
L26          0 L21 AND HUMANIZED ANTIBOD?

=> s l16 and humanized antibod?
L27        500 L16 AND HUMANIZED ANTIBOD?

=> s l27 and framework substitution
L28          0 L27 AND FRAMEWORK SUBSTITUTION

=> s l27 and substitution
L29         14 L27 AND SUBSTITUTION

=> dup remove l29
PROCESSING COMPLETED FOR L29
L30          14 DUP REMOVE L29 (0 DUPLICATES REMOVED)

=> s l30 and pd<20030123
   1 FILES SEARCHED...
   4 FILES SEARCHED...
L31          5 L30 AND PD<20030123

=> s l31 and pd<20030123
   2 FILES SEARCHED...
L32          5 L31 AND PD<20030123

=> d l32 1-5 cbib abs

L32  ANSWER 1 OF 5     MEDLINE on STN
1998428671.    PubMed ID: 9753694.   VEGF and the Fab fragment of a humanized
     neutralizing antibody: crystal structure of the complex at 2.4 A
     resolution and mutational analysis of the interface. Muller Y A; Chen Y;
     Christinger H W; Li B; Cunningham B C; Lowman H B; de Vos A M. (Department
     of Protein Engineering Genentech, Inc. 1 DNA Way, South San Francisco, CA
     94080, USA. ) Structure (London, England : 1993), (1998 Sep 15)
     Vol. 6, No. 9, pp. 1153-67.  Journal code: 101087697. ISSN: 0969-2126.
     Pub. country: ENGLAND: United Kingdom. Language: English.
AB   BACKGROUND: Vascular endothelial growth factor (VEGF) is a highly specific
     angiogenic growth factor; anti-angiogenic treatment through inhibition of
     receptor activation by VEGF might have important therapeutic applications
     in diseases such as diabetic retinopathy and cancer.  A neutralizing
     anti-VEGF antibody shown to suppress tumor growth in an in vivo
     murine model has been used as the basis for production of a
     humanized version.  RESULTS: We present the crystal structure of the
```

complex between VEGF and the Fab fragment of this humanized antibody, as well as a comprehensive alanine-scanning analysis of the contact residues on both sides of the interface. Although the VEGF residues critical for antibody binding are distinct from those important for high-affinity receptor binding, they occupy a common region on VEGF, demonstrating that the neutralizing effect of antibody binding results from steric blocking of VEGF-receptor interactions. Of the residues buried in the VEGF-Fab interface, only a small number are critical for high-affinity binding; the essential VEGF residues interact with those of the Fab fragment, generating a remarkable functional complementarity at the interface. CONCLUSIONS: Our findings suggest that the character of antigen-antibody interfaces is similar to that of other protein-protein interfaces, such as ligand-receptor interactions; in the case of VEGF, the principal difference is that the residues essential for binding to the Fab fragment are concentrated in one continuous segment of polypeptide chain, whereas those essential for binding to the receptor are distributed over four different segments and span across the dimer interface.

L32 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
2002:654964 Document No. 137:200261 Humanized anti-human gp39 antibodies for treating autoimmune diseases. Black, Amelia; Hanna, Nabil; Padlan, Eduardo A.; Newman, Roland A. (Idec Pharmaceuticals Corporation, USA). U.S. US 6440418 B1 20020827, 50 pp., Cont.-in-part of U. S. 6,001,358. (English). CODEN: USXXAM. APPLICATION: US 1997-925339 19970908. PRIORITY: US 1995-554840 19951107.
AB The present invention is directed to humanized antibodies which bind human gp39 and their use as therapeutic agents. These humanized antibodies are especially useful for treatment of autoimmune diseases, and as immunosuppressant during transplantation of heterologous cells, tissues or organs, cell therapy, and gene therapy.

L32 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
2001:904527 Document No. 136:36363 Non-agonistic antibodies to human gp39, compositions containing, and therapeutic use thereof. Anderson, Darrell R.; Pan, Li Zhen; Hanna, Nabil; Rastetter, William H.; Kloetzer, William S. (Idec Pharmaceuticals Corporation, USA). PCT Int. Appl. WO 2001094586 A2 20011213, 130 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2001-US18098 20010606. PRIORITY: US 2000-209584P 20000606.
AB The present invention is directed to antibodies which bind human gp39, are antagonistic of the CD40/CD40L interaction, but are non-agonistic of T-cell activation. The present invention is further directed to the use of these antibodies as therapeutic agents. These antibodies are especially useful for treatment of autoimmune diseases; and an immunosuppressant during transplantation of heterologous cells, tissues or organs, cell therapy, and gene therapy.

L32 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN
2001:78418 Document No. 134:146391 VGF polypeptides and methods of treating VGF-related disorders. Yan, Hai; Boone, Thomas C. (Amgen, Inc., USA). PCT Int. Appl. WO 2001007477 A1 20010201, 97 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN,

IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-US19701 20000719. PRIORITY: US 1999-PV144797 19990721.

AB The present invention provides novel VGF polypeptides and selective binding agents. The binding agents are monoclonal antibodies, polyclonal antibodies, antibody fragments, chimeric or humanized antibodies, CDR-grafted antibodies, and anti-idiotypic antibodies. The invention also provides host cells and methods for producing VGF polypeptides. The invention further provides VGF pharmaceutical compns. and methods for the diagnosis, treatment, amelioration, and/or prevention of diseases, conditions, and disorders associated with VGF polypeptides. The diseases include obesity, sterility, cachexia, eating disorder, AIDS-related complex, hypermetabolic conditions, hyperactivity, hypoactivity, hyperinsulin production, bulimia and anorexia nervosa. The pharmaceutical formulation agent is a carrier, adjuvant, solubilizer, stabilizer or antioxidant. The VGF polypeptide may also be modified with a water-soluble polymer; or may be expressed by cells encapsulated in permeable membrane for implantation.

L32 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2008 ACS on STN

1993:669018 Document No. 119:269018 Altered antibodies containing germ-line amino acids and their production. Winter, Gregory Paul; Carr, Francis Joseph; Harris, William Joseph (Scotgen Ltd., UK). PCT Int. Appl. WO 9317105 A1 19930902, 51 pp. DESIGNATED STATES: W: AT, AU, BB, BG, BR, CA, CH, CZ, DE, DK, ES, FI, GB, HU, JP, KP, KR, LK, LU, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SK, UA, US; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1993-GB363 19930219. PRIORITY: GB 1992-3459 19920219.

AB Altered antibodies, produced by recombinant DNA techniques, are described which are substantially immunosilent (have extremely low antigenicity) by virtue of their containing selected germ-line amino acid residues in place of somatically mutated residues in a native antibody. The altered antibody can have variable regions, which comprise complementarity-determining regions (CDR) conferring the capacity to bind a specific antigen, and a selected and predominantly germ-line framework produced e.g. by site-directed mutagenesis or gene synthesis. A gene for preparing the antibody is constructed from CDR-encoding nucleotide sequences with the proper antigen specificity and germ-line framework-encoding nucleotide sequences. Such antibodies are substantially not recognized as foreign by a recipient animal. Examples illustrate (1) the reshaping (humanization) of mouse monoclonal anti-lysozyme antibody D1.3 by transfer of CDRs to produce a corresponding humanized antibody with germ-line V region sequences; (2) conversion of antibody D1.3 to the germ-line equivalent of the same species; (3) conversion of a reshaped (mouse CDR-grafted) antibody to respiratory syncytial virus to its nearest germ-line equivalent; (4) grafting of CDRs of mouse monoclonal antibody 3a4D10 (to Clostridium perfringens α-toxin) onto a germ-line variable region framework from myeloma protein NEWM/REI.

=> s methods for production humanized antibodies and improving yield
L33 0 METHODS FOR PRODUCTION HUMANIZED ANTIBODIES AND IMPROVING YIELD

=> s improving yield of antibodies

```
L34          0 IMPROVING YIELD OF ANTIBODIES

=> s anti-VEGF antibod?
L35       1498 ANTI-VEGF ANTIBOD?

=> s l35 and humanized
L36         93 L35 AND HUMANIZED

=> s l36 and framework substitution
L37          0 L36 AND FRAMEWORK SUBSTITUTION

=> s l36 adn variable domain
MISSING OPERATOR L36 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s l36 and variable domain
L38          1 L36 AND VARIABLE DOMAIN

=> d l38 cbib abs

L38  ANSWER 1 OF 1  CAPLUS  COPYRIGHT 2008 ACS on STN
2003:656789   Document No. 139:196277  Antibody variants with faster antigen
     association rates for diagnostics and therapeutic uses.  Lowman, Henry B.;
     Marvin, Jonathan S. (Genentech, Inc., USA).  PCT Int. Appl. WO 2003068801
     A2 20030821, 81 pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ,
     BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,
     EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
     KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,
     NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
     TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG,
     CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR,
     NE, NL, PT, SE, SN, TD, TG, TR.  (English).  CODEN: PIXXD2.  APPLICATION:
     WO 2003-US4184 20030211.  PRIORITY: US 2002-355895P 20020211; US
     2002-409685P 20020910.
AB   Antibody variants with higher affinity to antigen are disclosed.  The
     antibody variants have one or more amino acid alteration(s) in or adjacent
     to at least one hypervariable region thereof which increase charge
     complementarity between the antibody variant and an antigen to which it
     binds.  Variants of anti-VEGF antibody
     Y0101, anti-tissue factor antibody D3H44 and anti-HER2 antibody 4D5 were
     prepared and tested.


=> s l36 and substitution
L39          3 L36 AND SUBSTITUTION

=> dup remove l39
PROCESSING COMPLETED FOR L39
L40          3 DUP REMOVE L39 (0 DUPLICATES REMOVED)

=> d l40 1-3 cbib abs

L40  ANSWER 1 OF 3  CAPLUS  COPYRIGHT 2008 ACS on STN
2003:656789   Document No. 139:196277  Antibody variants with faster antigen
     association rates for diagnostics and therapeutic uses.  Lowman, Henry B.;
     Marvin, Jonathan S. (Genentech, Inc., USA).  PCT Int. Appl. WO 2003068801
     A2 20030821, 81 pp.  DESIGNATED STATES: W:  AE, AG, AL, AM, AT, AU, AZ,
     BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC,
     EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP,
     KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO,
     NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
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TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-US4184 20030211. PRIORITY: US 2002-355895P 20020211; US 2002-409685P 20020910.

AB Antibody variants with higher affinity to antigen are disclosed. The antibody variants have one or more amino acid alteration(s) in or adjacent to at least one hypervariable region thereof which increase charge complementarity between the antibody variant and an antigen to which it binds. Variants of anti-VEGF antibody Y0101, anti-tissue factor antibody D3H44 and anti-HER2 antibody 4D5 were prepared and tested.

L40 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2008 ACS on STN

2000:351668 Document No. 133:16314 Antibody variants with higher binding affinity compared to parent antibodies. Chen, Yvonne M.; Lowman, Henry B.; Muller, Yves (Genentech, Inc., USA). PCT Int. Appl. WO 2000029584 A1 20000525, 110 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 1999-US27153 19991116. PRIORITY: US 1998-PV108945 19981118.

AB Antibody variants of parent antibodies are disclosed which have one or more amino acids inserted in a hypervariable region of the parent antibody and a binding affinity for a target antigen which is at least about two fold stronger than the binding affinity of the parent antibody for the antigen. Humanized anti-VEGF antibodies comprising heavy and light chain variable regions were prepared and tested for enhance binding activity. The prepared humanized antibodies or fragments are conjugated with detectable label or cytotoxic agent for diagnostic or therapeutic uses (e.g. for neoplasm or related disorders).

L40 ANSWER 3 OF 3 MEDLINE on STN

1998428671. PubMed ID: 9753694. VEGF and the Fab fragment of a humanized neutralizing antibody: crystal structure of the complex at 2.4 A resolution and mutational analysis of the interface. Muller Y A; Chen Y; Christinger H W; Li B; Cunningham B C; Lowman H B; de Vos A M. (Department of Protein Engineering Genentech, Inc. 1 DNA Way, South San Francisco, CA 94080, USA.) Structure (London, England : 1993), (1998 Sep 15) Vol. 6, No. 9, pp. 1153-67. Journal code: 101087697. ISSN: 0969-2126. Pub. country: ENGLAND: United Kingdom. Language: English.

AB BACKGROUND: Vascular endothelial growth factor (VEGF) is a highly specific angiogenic growth factor; anti-angiogenic treatment through inhibition of receptor activation by VEGF might have important therapeutic applications in diseases such as diabetic retinopathy and cancer. A neutralizing anti-VEGF antibody shown to suppress tumor growth in an in vivo murine model has been used as the basis for production of a humanized version. RESULTS: We present the crystal structure of the complex between VEGF and the Fab fragment of this humanized antibody, as well as a comprehensive alanine-scanning analysis of the contact residues on both sides of the interface. Although the VEGF residues critical for antibody binding are distinct from those important for high-affinity receptor binding, they occupy a common region on VEGF, demonstrating that the neutralizing effect of antibody binding results from steric blocking of VEGF-receptor interactions. Of the residues buried in the VEGF-Fab interface, only a small number are critical for high-affinity binding; the essential VEGF residues interact

with those of the Fab fragment, generating a remarkable functional complementarity at the interface. CONCLUSIONS: Our findings suggest that the character of antigen-antibody interfaces is similar to that of other protein-protein interfaces, such as ligand-receptor interactions; in the case of VEGF, the principal difference is that the residues essential for binding to the Fab fragment are concentrated in one continuous segment of polypeptide chain, whereas those essential for binding to the receptor are distributed over four different segments and span across the dimer interface.

=> s (simmons l?/au)
L41 1284 (SIMMONS L?/AU)

=> s l41 and improving yield
L42 1 L41 AND IMPROVING YIELD

=> d l42 cbib abs

L42 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
2004:633952 Document No. 141:156117 Methods for producing and improving yield of humanized or chimeric antibodies and fragments in cell culture. Simmons, Laura (Genentech, Inc., USA). PCT Int. Appl. WO 2004065417 A2 20040805, 161 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US1844 20040123. PRIORITY: US 2003-442484P 20030123.

AB The present invention provides methods for producing humanized antibodies and increasing the yield of antibodies and/or antigen binding fragments when produced in cell culture. The antibodies are anti-VEGF and anti-IgE antibodies. In one aspect of the invention, at least one framework region amino acid residue of the variable domain is substituted by a corresponding amino acid from a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain. In another aspect, an amino acid is placed at a position proximal to a cys residue that participates in an intrachain variable domain disulfide bond that corresponds to an amino acid found at that position in a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain.

=> s l41 and framework region
L43 1 L41 AND FRAMEWORK REGION

=> d l43 cbib abs

L43 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
2004:633952 Document No. 141:156117 Methods for producing and improving yield of humanized or chimeric antibodies and fragments in cell culture. Simmons, Laura (Genentech, Inc., USA). PCT Int. Appl. WO 2004065417 A2 20040805, 161 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW,

MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US1844 20040123. PRIORITY: US 2003-442484P 20030123.

AB The present invention provides methods for producing humanized antibodies and increasing the yield of antibodies and/or antigen binding fragments when produced in cell culture. The antibodies are anti-VEGF and anti-IgE antibodies. In one aspect of the invention, at least one framework region amino acid residue of the variable domain is substituted by a corresponding amino acid from a variable domain consensus sequence subgroup that has the most sequence identity with the HVRI and/or HVR2 amino acid sequence of the variable domain. In another aspect, an amino acid is placed at a position proximal to a cys residue that participates in an intrachain variable domain disulfide bond that corresponds to an amino acid found at that position in a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain.

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                  enhanced
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=> s method making
L1        1524 METHOD MAKING

=> s l1 adn humanized antibod?
MISSING OPERATOR L1 ADN
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> s method
L2    18771083 METHOD

=> s l2 and humanized antibod?
L3        1234 L2 AND HUMANIZED ANTIBOD?

=> s l3 and align?
L4           9 L3 AND ALIGN?

=> s l4 and hypervariable region
L5           0 L4 AND HYPERVARIABLE REGION

=> s l3 and heavy chain hypervariable region
L6           0 L3 AND HEAVY CHAIN HYPERVARIABLE REGION

=> s l3 and hypervariable region
L7          13 L3 AND HYPERVARIABLE REGION

=>  s l7 and human subgroup
L8           0 L7 AND HUMAN SUBGROUP

=> s l7 and consensus sequence
L9           2 L7 AND CONSENSUS SEQUENCE

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10          2 DUP REMOVE L9 (0 DUPLICATES REMOVED)

=> d l10 1-2 cbib abs

L10  ANSWER 1 OF 2  CAPLUS  COPYRIGHT 2008 ACS on STN
2004:633952   Document No. 141:156117  Methods for producing and
     improving yield of humanized or chimeric antibodies and fragments in cell
     culture.  Simmons, Laura (Genentech, Inc., USA).  PCT Int. Appl. WO
     2004065417 A2 20040805, 161 pp.  DESIGNATED STATES: W:  AE, AE, AG, AL,
     AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY,
     BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK,
     DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR,
     HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR,
     KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW,
     MX, MX, MZ, MZ, NA, NI.  (English).  CODEN: PIXXD2.  APPLICATION: WO
     2004-US1844 20040123.  PRIORITY: US 2003-442484P 20030123.
AB   The present invention provides methods for producing
     humanized antibodies and increasing the yield of
```

antibodies and/or antigen binding fragments when produced in cell culture. The antibodies are anti-VEGF and anti-IgE antibodies. In one aspect of the invention, at least one framework region amino acid residue of the variable domain is substituted by a corresponding amino acid from a variable domain consensus sequence subgroup that has the most sequence identity with the HVRI and/or HVR2 amino acid sequence of the variable domain. In another aspect, an amino acid is placed at a position proximal to a cys residue that participates in an intrachain variable domain disulfide bond that corresponds to an amino acid found at that position in a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain.

L10 ANSWER 2 OF 2 SCISEARCH COPYRIGHT (c) 2008 The Thomson Corporation on STN

2005:283592 The Genuine Article (R) Number: 903GF. Functional humanization of an anti-CD30 Fab fragment for the immunotherapy of Hodgkin's lymphoma using an in vitro evolution approach. Schlapschy M; Gruber H; Gresch O; Schafer C; Renner C; Pfreundschuh M; Skerra A (Reprint). Tech Univ Munich, Lehrstuhl Biol Chem, D-85350 Freising Weihenstephan, Germany (Reprint); CRMP Univ Saarland, Sch Med, D-66421 Homburg, Germany. skerra@wzw.tum.de. PROTEIN ENGINEERING DESIGN & SELECTION (DEC 2004) Vol. 17, No. 12, pp. 847-860. ISSN: 1741-0126. Publisher: OXFORD UNIV PRESS, GREAT CLARENDON ST, OXFORD OX2 6DP, ENGLAND. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB CD30, the so-called Reed-Sternberg antigen, constitutes a promising cell-specific target for the treatment of Hodgkin's lymphoma. Starting from the previously characterized cognate HRS3 mouse monoclonal antibody, the bacterially produced functional Fab fragment was humanized by grafting the CDRs from the mouse antibody framework on to human immunoglobulin consensus sequences. This procedure led to a 10-fold decreased antigen affinity, which surprisingly was found to be mainly due to the V-H domain. To improve the antigen-binding activity, an in vitro evolution strategy was employed, wherein random mutations were introduced into the humanized V-H domain by means of error-prone PCR, followed by a filter sandwich Escherichia coli colony screening assay for functional Fab fragments using a recombinant extracellular domain of the CD30 antigen. After three cycles of in vitro affinity maturation, the optimized Fab fragment huHRS3-V-H-EP3/1 was identified, which carried four exchanged residues within or close to the V-H CDRs and had an affinity that was almost identical with that of the murine HRS3 Fab fragment. The resulting humanized Fab fragment was fully functional with respect to CD30 binding both in ELISA with the recombinant antigen and in FACS experiments with CD30-positive L540CY cells. In the light of the previously successful clinical application of an alphaCD30 x alphaCD16 bispecific mouse quadroma antibody derived from HRS3, the humanized Fab fragment comprises an important step towards the construction of a fully recombinant therapeutic agent. The combination of random mutagenesis and colony filter screening assay that was successfully applied here should be generally useful as a method for the rapid functional optimization of humanized antibody fragments.

=> s l3 and "HVR1"
L11 1 L3 AND "HVR1"

=> d l11 cbib abs

L11 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN

2004:633952 Document No. 141:156117 Methods for producing and improving yield of humanized or chimeric antibodies and fragments in cell culture. Simmons, Laura (Genentech, Inc., USA). PCT Int. Appl. WO

2004065417 A2 20040805, 161 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US1844 20040123. PRIORITY: US 2003-442484P 20030123.

AB The present invention provides methods for producing humanized antibodies and increasing the yield of antibodies and/or antigen binding fragments when produced in cell culture. The antibodies are anti-VEGF and anti-IgE antibodies. In one aspect of the invention, at least one framework region amino acid residue of the variable domain is substituted by a corresponding amino acid from a variable domain consensus sequence subgroup that has the most sequence identity with the HVRI and/or HVR2 amino acid sequence of the variable domain. In another aspect, an amino acid is placed at a position proximal to a cys residue that participates in an intrachain variable domain disulfide bond that corresponds to an amino acid found at that position in a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain.

=> s L3 and "HVR2"
L12 1 L3 AND "HVR2"

=> d l12 cbib abs

L12 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2008 ACS on STN
2004:633952 Document No. 141:156117 Methods for producing and improving yield of humanized or chimeric antibodies and fragments in cell culture. Simmons, Laura (Genentech, Inc., USA). PCT Int. Appl. WO 2004065417 A2 20040805, 161 pp. DESIGNATED STATES: W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI. (English). CODEN: PIXXD2. APPLICATION: WO 2004-US1844 20040123. PRIORITY: US 2003-442484P 20030123.

AB The present invention provides methods for producing humanized antibodies and increasing the yield of antibodies and/or antigen binding fragments when produced in cell culture. The antibodies are anti-VEGF and anti-IgE antibodies. In one aspect of the invention, at least one framework region amino acid residue of the variable domain is substituted by a corresponding amino acid from a variable domain consensus sequence subgroup that has the most sequence identity with the HVRI and/or HVR2 amino acid sequence of the variable domain. In another aspect, an amino acid is placed at a position proximal to a cys residue that participates in an intrachain variable domain disulfide bond that corresponds to an amino acid found at that position in a variable domain consensus sequence subgroup that has the most sequence identity with the HVR1 and/or HVR2 amino acid sequence of the variable domain.

=> s l3 and improved yield
L13 0 L3 AND IMPROVED YIELD

=> s l2 and improved yield
L14 2042 L2 AND IMPROVED YIELD

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=> s l14 and antibody production
L15             4 L14 AND ANTIBODY PRODUCTION

=> dup remove l15
PROCESSING COMPLETED FOR L15
L16             4 DUP REMOVE L15 (0 DUPLICATES REMOVED)

=> d l16 1-4 cbib abs

L16  ANSWER 1 OF 4  BIOSIS  COPYRIGHT (c) 2008 The Thomson Corporation  on STN
2006:504520  Document No.: PREV200600507869. Hapten synthesis and development
     of polyclonal antibody-based multi-sulfonamide immunoassays. Zhang,
     Hongyan; Duan, Zhenjuan; Wang, Lei; Zhang, Yan; Wang, Shuo [Reprint
     Author]. Tianjin Univ Sci and Technol, Tianjin Key Lab Food Nutr and
     Safety, Fac Food Engn and Biotechnol, Tianjin 300222, Peoples R China.
     s.wang@tust.edu.cn. Journal of Agricultural and Food Chemistry, (JUN 28
     2006) Vol. 54, No. 13, pp. 4499-4505.
     CODEN: JAFCAU. ISSN: 0021-8561. Language: English.
AB   This paper reports the synthesis of five sulfonamide derivatives, the
     production of broad-specificity polyclonal antibodies for immunoassay of
     sulfonamides, and the analysis of milk samples by developed assay.  The
     three-step synthesis procedure reported in most of the literature was
     adopted and modified in this study.  In the procedure, the purification of
     the intermediate was avoided and the time of synthesis was shortened from
     > 20 to 6-9 h with improved yields.  This
     method is generally applicable to the synthesis of haptens
     containing the common structure of sulfonamides.  Three haptens were
     coupled to keyhole limpet hemocyanin, and polyclonal antibodies were
     obtained from rabbits immunized with these conjugates.  Using the
     antibodies obtained, from one of these was developed an enzyme-linked
     immunosorbent assay (ELISA) based on the competition between free
     sulfonamides and the hapten-horseradish peroxidase (HRP) conjugates.  The
     hapten-HRP conjugate giving the best competitive results and 11
     structurally different sulfonamides showed 50% inhibition at
     concentrations of < 100 ng mL(-1).  After removal of the protein with
     acetone, milk samples were analyzed by ELISA directly; a matrix effect
     could be avoided when a 1: 20 dilution with phosphate-buffered saline was
     used, and 104-131% recoveries of spiked samples were obtained.  The
     developed immunoassay is suitable to determine sulfisozole, sulfathiazole,
     sulfameter, sulfamethoxypyridazine, sulfapyridine, and sulfamethizole
     below the maximum residue limit in milk (100 ng mL(-1) of total
     sulfonamides) rapidly and reliably.

L16  ANSWER 2 OF 4  CAPLUS  COPYRIGHT 2008 ACS on STN
2005:245422  Document No. 142:428384  Production and isolation of IgY antibody
     raised against a lectin obtained from Maackia fauriei.  Chung, Young Yun;
     Jung, Eui Cha; Lee, Hyun Jung; Kim, Hahyung (College of Pharmacy,
     Chung-Ang University, Seoul, 156-756, S. Korea).  Yakhak Hoechi, 49(1),
     6-10 (Korean) 2005.  CODEN: YAHOA3.  ISSN: 0377-9556.  Publisher:
     Pharmaceutical Society of Korea.
AB   IgY obtained from chicken as the immunization host brings several
     advantages to antibody production, such as
     improved yield, lower cost, longer stability, and higher
     specificity than mammalian Ig.  In the present study, we attempted to
     produce IgY against a sialic acid-binding lectin, Maackia fauriei
     agglutinin (MFA), from egg yolk of white Leghorn hens.  For the isolation
     of IgY from egg yolk, we applied a water dilution method.  The
     weekly yield of IgY was determined by ELISA, with a final yield of anti-MFA IgY
     from total IgY of approx. 1%.  The IgY was used to prepare IgY-affinity
     column conjugated with CNBr-activated Sepharose 4B, which resulted in the
     lectin being successfully purified in a single step from Maackia fauriei.
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This purified lectin exhibited the same hemagglutination activity as lectin purified using conventional purification methods.

L16 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2008 ACS on STN
1989:435534 Document No. 111:35534 Original Reference No. 111:6013a,6016a Purification of human muscle phosphoglycerate mutase by fast protein liquid chromatography based on hydrophobic interactions. Edwards, Robert J.; Carter, Nick D.; Jeffery, Stephen; Yates, Sarah (Dep. Clin. Pharmacol., R. Postgrad. Med. Sch., London, W12 0NN, UK). Journal of Chromatography, 490(2), 424-31 (English) 1989. CODEN: JOCRAM. ISSN: 0021-9673.
AB Hydrophobic interaction chromatog. provides an alternative means of purification of proteins and has been especially useful here for the purification of phosphoglycerate mutase (PGAM) from human muscle. The method, using a Phenyl-Superose column, proved to be fast, reproducible, and thus superior to the more commonly used methods of hydroxylapatite and gel-permeation chromatog. for the purification of this enzyme. This is the 1st report of a successful purification of human PGAM. The method was rapid, using only 2 purification procedures, and had a relatively high yield (50%) compared with the purification of muscle PGAM from the muscle of pig and other species, where typical yields were 28% after 4 separation procedures. The improved yield was obtained even where the quantity available was small and the quality was poor. Sufficient quantities of PGAM for antibody production were obtained. The method of hydrophobic interaction chromatog. thus provides a suitable means to purify this basic protein and retain enzyme activity.

L16 ANSWER 4 OF 4 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
1966:53580 Document No.: PREV19664700053582; BA47:53582. Protective antigens from El Tor virbrios. 2. Responses in animals and man to partially purified Ogawa lipopolysaccharide antigen. WATANABE, YOSHIKAZU; VERWEY, W. F.; MACDONALD, E. M.. Div. Commun. Dis., World Health Organ., Geneva, Switz.. BULL WORLD HEALTH ORGAN, (1965) Vol. 52, No. 6, pp. 823-831. Language: Unavailable.
AB A previous report described the extraction and purification of a mouse-protective lipopolysaccharide antigen from culture supernatants of an El Tor vibrio of the Ogawa subtype. The chemical procedures for complete purification were complex, and considerable antigen was lost. The present paper describes a simpler method of obtaining an antigen of only slightly less purity in considerably improved yield. The method appears to be feasible for the preparation of an antigen that might be suitable for extensive immunization studies in humans. The antigen has been compared with the purified lipopolysaccharide and the Ogawa reference vaccine supplied by the National Institutes of Health with respect to active protection in mice, toxicity in mice and rabbits, and ability to produce passive mouse-protective antibody and vibriocidal antibody in rabbits. It has also been administered to a small number of volunteers in whom it was studied for its reaction-producing properties and its ability to produce agglutinin, vibriocidin and passive mouse-protective antibody. Little toxicity was found at dosages that induced very significant antibody production, and antibody remained elevated for at least 6 months. ABSTRACT AUTHORS: Authors

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